frequently and have less severe cardiopulmonary manifestations.<sup>3</sup> Even in the event of inclusion of false-positive results in the presented data, the financial burden remains the same; the reported cases are contributing to an overall increasing trend in health-care cost and use.

Sean B. Smith, MD Chicago, IL

**AFFILIATIONS:** From the Department of Pulmonary and Critical Care Medicine, Northwestern University.

**FINANCIAL/NONFINANCIAL DISCLOSURES:** See earlier cited article for author conflicts of interest.

CORRESPONDENCE TO: Sean B. Smith, MD, Pulmonary and Critical Care Medicine, Feinberg School of Medicine, Northwestern University, 660 N Westmoreland Rd, Lake Forest, IL 60045; e-mail: sean@northwestern.edu

Copyright © 2016 Published by Elsevier Inc under license from the American College of Chest Physicians.

**DOI:** http://dx.doi.org/10.1016/j.chest.2016.04.023]

## References

- Hutchinson BD, Navin P, Marom EM, Truong MT, Bruzzi JF. Overdiagnosis of pulmonary embolism by pulmonary CT angiography. AJR Am J Roentgenol. 2015;205(2):271-277.
- Smith SB, Geske JB, Kathuria P, et al. Analysis of national trends in admissions for pulmonary embolism. Chest. 2016;150(1):35-45.
- 3. Peiman S, Abbasi M, Allameh SF, Asadi G, Abtahi H, Safavi E. Subsegmental pulmonary embolism: a narrative review. *Thromb Res.* 2016;138:55-60.

# A Global Survey on Whole Lung Lavage in Pulmonary Alveolar Proteinosis



### To the Editor:

Whole lung lavage (WLL) is the current standard of care to treat pulmonary alveolar proteinosis (PAP), a rare

## TABLE 1 ] Centers Participating in the Survey

Center	WLL	LSBL	Adult	Pediatric
Sheffield Children's Hospital, Sheffield, England	Х	Х		Х
Royal Brompton Hospital, London, England	X	Х	Х	Х
Sheba Medical Centre, Tel-Hashomer, Tel Aviv University, Tel Aviv, Israel	X		Х	Х
Children's Hospital Boston, Boston, MA, USA	X			Х
Kinderklinik und Kinderpoliklinik im, University of Munich, Munich, Germany	X	Х		Х
Cincinnati Children's Hospital, Cincinnati, OH, USA	X	Х		Х
Fondazione IRCCS Policlinico San Matteo, Pavia, Italy	X		Х	
University of North Carolina at Chapel Hill, Chapel Hill, NC, USA		Х		Х
Hacettepe University, Ankara, Turkey		Х		X
University of the Witwatersrand, Johannesburg, South Africa		Х		Х
Pavlov State Medical University, St. Petersburg, Russia	X	Х	Х	
NHO Kinki-Chuo Chest Medical Centre, Osaka, Japan	Х	Х	Х	
University Medical College, Hangzhou, Zhejiang, China	X	Х	Х	
Lungenklinik Grosshandorf, Grosshandorf Germany	Х		Х	
University Hospital, Olomouc, Czech Republic	X		Х	
Asklepios-Fachkliniken München Gauting, Gauting, Germany	X		Х	
Helsinki University Central Hospital, Helsinki, Finland	X		Х	
Cork University Hospital, Cork, Ireland	Х		Х	
Care Medicine Thoraxklinik, Heidelberg, Germany	X		Х	
Serviço de Pneumologia-Hospital São João-Porto, São João-Porto, Portugal	Х		Х	
Ruhrlandklinik-University of Duisburg Essen, Essen, Germany	X		Х	
University Hospital, Zurich, Switzerland	Х		Х	
Hopital Louis Pradel, Lyon, France	X		Х	
Tokyo Medical University Hachioji Medical Centre, Hachioji City, Japan	Х		Х	
Kantonsspital Aarau, Aarau Switzerland	Х		Х	
St. Antonius Hospital, Nieuwegein, The Netherlands	Х		Х	
Kempten-Oberallgäu Hospital, Immenstadt, Germany	X		Х	Х

 $LSBL = lobar/segmental\ bronchoscopic\ lavage;\ WLL = whole\ lung\ lavage.$ 

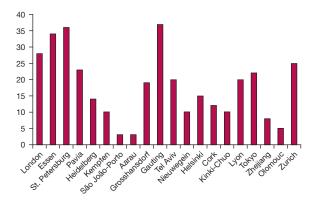


Figure 1 – Years of experience at each center in performing whole lung lavage (WLL) in adult patients with pulmonary alveolar proteinosis (PAP).

respiratory syndrome characterized by the accumulation of lipoproteinaceous material in alveoli, which impairs oxygen uptake and causes respiratory failure.<sup>1,2</sup>

We present a clinical practice survey on WLL, which was conducted by means of a questionnaire.<sup>3</sup> Two major considerations prompted us to perform the present survey: (1) even if WLL for treatment of PAP was described more than 50 years ago,<sup>4</sup> it is still an elitist procedure with poor accessibility and (2) the WLL procedure is, in most cases, the result of a long-term process of self-education, with progressive improvement of the lavage technique.<sup>5</sup>

An international committee of physicians performing WLL or caring for patients with PAP, or both, developed the survey questionnaire, which comprises sections for physicians performing only WLL and physicians performing only lobar/segmental bronchoscopic lavage (LSBL), or physicians performing both WLL and LSBL.

Respondents were from 20 centers in 14 countries performing WLL in adults and 10 centers in 6 countries performing WLL in pediatric patients (Table 1). The mean ( $\pm$  SD) duration of experience was 18  $\pm$  11 years (Fig 1).

The results show that WLL in adults is performed almost universally using general anesthesia with a double-lumen tracheal tube in two consecutive sessions (one lung per session), with an interval of 1 to 2 weeks between WLL procedures observed by 50% of centers. Other common aspects are the use of saline warmed to 37°C and drainage of instilled fluid by gravity. The amount of fluid used to perform the WLL is a critical aspect. The volume of saline aliquots infused varies greatly (800 mL of warm saline on average), and a great

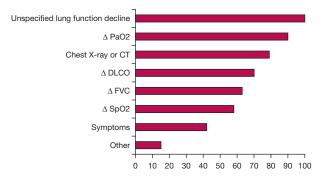


Figure 2 – Observed frequency (%) of indication for WLL among the centers. More than one answer was possible;  $\Delta =$  decline from baseline.

variability exists for the total volume used per lung, with a range from 5 to 40 L.

Most (14 of 20) centers use chest percussion to emulsify the PAP sediment to improve therapeutic efficiency. However, the method and timing vary greatly. Ten centers (50%) use manual chest percussion and four (20%) centers use mechanical percussion.

Indications for WLL vary among centers (Fig 2). There is also a great discrepancy in the choice of position: supine positioning was chosen by 50% of centers and rotation and change of positions was performed by 7 centers.

This international survey found that WLL is safe and effective as therapy for PAP and represents a first step in developing an evidence-based, best-practice approach to standardizing WLL therapy for PAP.

Ilaria Campo, PhD Maurizio Luisetti, MD, PhD Pavia, Italy Matthias Griese, MD Munich, Germany Bruce C. Trapnell, MD Cincinnati, OH Francesco Bonella, MD, PhD Essen, Germany Jan C. Grutters, MD, PhD Nieuwegein, The Netherlands Koh Nakata, MD, PhD Niigata, Japan Coline H. M. Van Moorsel, PhD Nieuwegein, The Netherlands Ulrich Costabel, MD, PhD Essen, Germany Vincent Cottin, MD, PhD Lyon, France Toshio Ichiwata, MD, PhD Tokyo, Japan

Yoshikazu Inoue, MD, PhD
Osaka, Japan
Antonio Braschi, MD, PhD
Giacomo Bonizzoni, MD
Giorgio A. Iotti, MD
Carmine Tinelli, MD
Giuseppe Rodi, MD
Pavia, Italy
for the WLL International Study Group

AFFILIATIONS: From the Pneumology Unit (Drs Campo, Luisetti and Bonizzoni), IRCCS San Matteo Hospital Foundation and University of Pavia; Kinderklinik und Kinderpoliklinik im Dr. von Haunerschen Kinderspital (Dr Griese), University of Munich; Translational Pulmonary Science Center (Dr Trapnell), Cincinnati Children's Hospital; Interstitial and Rare Lung Disease Unit (Drs Bonella and Costabel), Ruhrlandklinik University Hospital, University of Duisburg-Essen; Centre of Interstitial Lung Diseases (Drs Grutters and Van Moorsel), St. Antonius Hospital Nieuwegein; Niigata University Medical and Dental School (Dr Nakata); National Reference Centre for Rare Pulmonary Disease (Dr Cottin), Hopital Louis Pradel; Tokyo Medical University Hachioji Medical Center (Dr Ichiwata); Department of Diffuse Lung Diseases and Respiratory Failure (Dr Inoue), Clinical Research Centre, National Hospital Organization Kinki-Chuo Chest Medical Centre; Department of Anesthesiology and Intensive Care (Drs Braschi, Iotti, and Rodi), IRCCS San Matteo Hospital Foundation, University of Pavia; and Clinical Epidemiology and Biometric Unit (Dr Tinelli), IRCCS San Matteo Hospital Foundation.

Drs Campo and Luisetti contributed equally to this manuscript. **FINANCIAL/NONFINANCIAL DISCLOSURES:** None disclosed. **FUNDING/SUPPORT:** This study was supported by a grant from European Union E-Rare JTC 2009: EuPAPnet.

CORRESPONDENCE TO: Ilaria Campo, PhD, Laboratorio di Biochimica e Genetica S.C. Pneumologia, Fondazione IRCCS Policlinico San Matteo, via Taramelli 5, 27100-Pavia, Italy; e-mail: i.campo@smatteo.pv.it

Copyright @ 2016 American College of Chest Physicians. Published by Elsevier Inc. All rights reserved.

**DOI:** http://dx.doi.org/10.1016/j.chest.2016.04.030

## Acknowledgments

**Guarantor statement:** Ilaria Campo takes responsibility for the content of the manuscript, including the data and analysis.

**Role of Sponsors:** The sponsor had no role in the design of the study, the collection and analysis of the data, or the preparation of the manuscript.

**Collaborators:** The complete list of the members of the Whole Lung Lavage International Study Group is available in e-Table 1.

**Other contributions:** This project was initiated by the late Dr. Maurizio Luisetti (1953-2014) whose passion for research and advocacy for people affected by rare diseases, including PAP, and recognition of the need and importance of optimizing and standardizing the practice of WLL, resulted in this project.

**Additional information:** The e-Table can be found in the Supplemental Materials section of the online article.

### References

- Trapnell BC, Whitsett JA, Nakata K. Pulmonary alveolar proteinosis. N Engl J Med. 2003;349:2527-2539.
- Luisetti M, Kadija Z, Mariani F, Rodi G, Campo I, Trapnell BC. Therapy options in pulmonary alveolar proteinosis. *Ther Adv Respir Dis.* 2010;4:239-248.
- Luisetti M. Call for an international survey on therapeutic lavage for pulmonary alveolar proteinosis. Eur Respir J. 2012;39:1049.

- Ramirez J, Schultz RB, Dutton RE. Pulmonary alveolar proteinosis: a new technique and rationale for treatment. *Arch Intern Med.* 1963; 112:419-431.
- Seymour JF, Presneill JJ. Pulmonary alveolar proteinosis: progress in the first 44 years. Am J Respir Crit Care Med. 2002;166: 215-235.

# Prediction of Mortality in Pulmonary Embolism Based on Left Atrial Volume Measurements



## Do Indexed Values Matter?

### To the Editor:

We read the paper by Aviram et al<sup>1</sup> published in *CHEST* (March 2016) with great interest and congratulate the authors on their excellent work. Using CT pulmonary angiography (CTPA), the study demonstrated an association of decreased left atrial (LA) volumes and mortality in patients with acute pulmonary embolism (PE), in which it is theorized that a decrease in right ventricular stroke volume leads to underfilling of the left atrium. These findings are corroborated by previous studies using echocardiography and advocate the need for further studies using CTPA to risk stratify high-risk patients with PE.

The current analysis suggests that patients with a smaller LA volume, by nongated CTPA, have a higher risk of mortality after PE. Given the known heterogeneity of LA volumes according to body surface area (BSA), it would be helpful to index LA volumes to BSA. Studies have demonstrated that LA size was larger with increasing body size and male sex, potentially explaining up to 29% of LA size variability. Additionally, race should be taken into account because of the significantly greater dimensions among whites,3 as well as evident racial disparities with PE mortality. 4 To partially account for patient BSA, right atrial to LA ratio was used by Chow et al<sup>5</sup> to predict long-term mortality; however, this association was not as definitive. The CTPA images are nongated and represent data from a range of cardiac phases, with reduced filling time at higher heart rates. This may partly account for why the right atrial to LA volume ratio association is not as strong by CTPA. The increasing availability of advanced CT scanner systems will enable excellent-quality gated PE examinations, making metrics derived from chamber volumes more reliable.

Despite the population-associated risk of low LA volume with increased mortality, the interquartile ranges overlap significantly, making LA volume difficult to apply to a