ABSTRACT (provisional v1-25-03-2022) - PLUG meeting presentation (20 or 27th April 2022)

TITLE: *Continuous slow-flow inflation method to build esophageal balloon PV curve: a step toward a simple and refined method to calibrate air-filled esophageal catheter for accurate trans-pulmonary monitoring?*

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This abstract shows preliminary results available at this time, based on a subset of study patient sample. Further analysis is in progress, which could be presented in a more completed and/or refined version within few weeks.

INTRODUCTION

Trans-pulmonary pressure (TPP) monitoring is increasingly advocated in a way to capture mechanical stress applied to injured lungs exposed to mechanical ventilation, with potentially additional hit related to inappropriate ventilator settings (so called VILI and/or acceptable mechanical power) (1,2). Moreover, TPP paradigm appears to be a pivotal physiological variable at bedside, likely to guide individual ventilation strategy, even if robust evidence is still awaited (3,4). TPP needs to asses pleural pressure for which esophageal pressure (Peso) is now considered as an acceptable proxy (5). However, for accurate Peso measurement, refined calibration has been recently proposed and seems mandatory for volume guidance with available device, based on air-filled balloon catheters (6). Balloon volume target seem to be difficult to standardize and precise Peso monitoring is crucial to infer accurate TPP and inherent computation of the partitioned mechanics of the respiratory system (7). The method proposed by Mojoli et al, and colleagues, even necessary, remains cumbersome which may limit wide adoption of TPP monitoring in clinical practice.

AIM OF THIS STUDY

We describe an original method to build pressure-volume curve of the air filled esophageal catheter balloon in a way to simplify calibration step for Peso and TPP monitoring in ARDS patients. The PV curve was captured dynamically during a slow-flow inflation of the balloon and informative variables were extracted and computationally analyzed based on high-resolution signal. We compared experimental protocol values of targeted volume (VbestXP) to reference method (so called occlusion test, OT) in a subset of patient with high-resolution continuous technique, and put into perspective in whole population (retrospective analysis of OT from complete step by step calibration procedure, as proposed by Mojoli et al, see Ref 6).

METHOD & RESULTS

Study population: severe ARDS patients eligible to muscular paralysis with NMR (*this study is ancillary technical part of a study dealing with curare impact on respiratory mechanics – TD4-curares study, institutionally approved and registered*).

Experimental procedure: Esophageal catheter – Nutrivent®, Sidam, Italy - was inserted by nostril then appropriate positioning was performed and checked as recommended (1,2). The air-filed syringe was connected to the Peso monitoring circuit using a Y-branch. After zeroing, balloon inflation was performed at a rate of 100 ml/h. The continuous Peso recorded along with balloon volume inflation until the maximal loaded volume of 10 ml (FIG1). Data were recorded with Fluxmed, MBMed® device and post-hoc off-line signal processing performed using with Graphysio® and Matlab® with engineering of codes for mathematical analysis to identify main variables useful for volume guidance (i.e. Vbest, Vmin, Eew, FIG2). Calibration of Peso catheter was then completed with occlusion test manoeuver (OT) as recommended (1,6), and experimental variables were compared to gold-standard which was the ratio of increment of Peso to increment in airway pressure during occlusion and compression of the chest: dPeso/dPaw; the closest to 1.0 ratio is considered as to define the most suitable volume balloon to assess precise Peso values, see Ref 1 and FIG1 and 2 for details.

Results: Five patients were included in this pilot phase of our study, with one patient analyzed 4 times during evolving Acute Respiratory Syndrome (to assess intra-individual variability). We show here first results extracted from analysis of the first 5 patients, in a proof-of-concept perspective. Results are presented graphically and resumed as means +/-SD (range). Briefly we observed that:

(i) PV curve patterns were reproducible and similar to graphical and biomechanical framework described by Mojoli et al in its volume step by step calibration *princeps* study (FIG 2)

(ii) Vbest: was identifiable most of time (as others variables like Vmin and Eew); was highly variable and individually different to standardized fixed volume of 4 ml (TAB); corresponded to the OT ratio closest to 1.00, in the limit of the sample

(iii) in whole population of the Peso monitoring cohort (n=15), volume eligibility based on qualifying OT as reference (ratio comprised between classical range of 0,8 to 1,2) was large and leaded to wide dispersion of Peso values (TAB)

DISCUSSION & PERSPECTIVES

We aimed at proposing a novel approach to simplify calibration of esophageal pressure. Preliminary results from our experimental method agree with Mojoli and colleagues reference work. Furthermore, our approach also collects other key variables for volume guidance such as Vmin or Eew. These preliminary results suggest that a simplified volume guidance is possible with the technique we developed, although our sample size has to be increased for further validation.

Inter-individual variability for suitable balloon volume may be confirmed in larger cohort, as first reported in one calibration study with relatively homogeneous population (6).

Following validation of our method, next step is to develop an on-line analysis for PV curve based on automatic volume calibration on dedicated respiratory monitoring device or implemented in ventilators. Such user-friendly Peso monitoring technique would promote its use at bedside.

Moreover, and interestingly, choice of a volume based on a unique acceptable OT (ratio comprised between 0.8-1.2) to validate position and presumed appropriate volume is likely to lead to variable Peso and TPP values. Theses preliminary observations, if confirmed, may challenge usual reference method for Peso monitoring as prescribed (1,7,8), and may reinforce Mojoli et al perspective in a way to embrace the most accurate Peso values likely to limit TPP technical assessment pitfalls. To conclude, we hope advanced Peso monitoring, could evolve from an appealing pathophysiological concept to a more desirable and simplified concrete clinical issue, as what our first insights may help to pursue.

REFERENCES (n=8)

(1) Esophageal and transpulmonary pressure in the clinical setting: meaning, usefulness and perspectives. Tommaso Mauri 1, Takeshi Yoshida 2 3 4, Giacomo Bellani 5, Ewan C Goligher 6 7 8, Guillaume Carteaux 9 10, Nuttapol Rittayamai 11 12 8, Francesco Mojoli 13, Davide Chiumello 1 14, Lise Piquilloud 15 16, Salvatore Grasso 17, Amal Jubran 18, Franco Laghi 18, Sheldon Magder 19, Antonio Pesenti 1 14, Stephen Loring 20, Luciano Gattinoni 1 14, Daniel Talmor 20, Lluis Blanch 21, Marcelo Amato 22, Lu Chen 12 8, Laurent Brochard 23 24, Jordi Mancebo 25, PLeUral pressure working Group (PLUG—Acute Respiratory Failure section of the European Society of Intensive Care Medicine) Intensive Care Med. 2016 Sep;42(9):1360-73

(2) Targeting transpulmonary pressure to prevent ventilator-induced lung injury. Gattinoni L, Giosa L, Bonifazi M, Pasticci I, Busana M, Macri M, Romitti F, Vassalli F, Quintel M. Expert Rev Respir Med. 2019 Aug;13(8):737-746.

(3) ECMO criteria for influeneza A (H1N1)-associated ARDS: role of the transpulmonary pressure 1 Salvatore Grasso, Pierpaolo Terragni, Alberto Birocco, Rosario Urbino, Lorenzo Del Sorbo, Claudia Filippini, Luciana Mascia, Antonio Pesenti, Alberto Zangrillo, Luciano Gattinoni, and V. Marco Ranieri. Intensive Care Medicine,38(3),2012

(4) Effect of Esophageal Pressure-guided Positive End-Expiratory Pressure on Survival from Acute Respiratory Distress Syndrome: A Risk-based and Mechanistic Reanalysis of the EPVent-2 Trial. Sarge T, Baedorf-Kassis E, Banner-Goodspeed V, Novack V, Loring SH, Gong MN, Cook D, Talmor D, Beitler JR; EPVent-2 Study Group. Am J Respir Crit Care Med. 2021 Nov 15;204(10):1153-1163

(5) Esophageal Manometry and Regional Transpulmonary Pressure in Lung Injury. Takeshi Yoshida1,2,3, Marcelo B. P. Amato4, Domenico Luca Grieco1,2,5,6, Lu Chen1,2, Cristhiano A. S. Lima4, Rollin Roldan4,7, Caio C. A. Morais4, Susimeire Gomes4, Eduardo L. V. Costa4, Paulo F. G. Cardoso8, Emmanuel Charbonney6,9, Jean-Christophe M. Richard6,10, Laurent Brochard1,3,6, and Brian P. Kavanagh2,3 Am J Respir Crit Care Med Vol 197, Iss 8, pp 1018–1026, Apr 15, 2018

(6) In vivo calibration of esophageal pressure in the mechanically ventilated patient makes measurements reliable. Francesco Mojoli1,2*, Giorgio Antonio Iotti1, Francesca Torriglia2, Marco Pozzi1, Carlo Alberto Volta3, Stefania Bianzina2, Antonio Braschi1,2 and Laurent Brochard4,5 Critical Care (2016) 20:98

(7) Mechanical Ventilation Guided by Uncalibrated Esophageal Pressure May Be Potentially Harmful . Gianmaria Cammarota, M.D., Ph.D., Gianluigi Lauro, M.D., Erminio Santangelo, M.D., Ilaria Sguazzotti, M.D., Raffaella Perucca, M.D., Federico Verdina, M.D., Ester Boniolo, M.D., Riccardo Tarquini, M.D., Elena Bignami, M.D., Silvia Mongodi, M.D., Ph.D., M.Sc., Eric Arisi, M.D., Anita Orlando, M.D., Ph.D., Francesco Della Corte M.D., Rosanna Vaschetto, M.D., Ph.D., M.Sc., Francesco Mojoli, M.D. Anesthesiology 2020; Jul;133(1):145-153

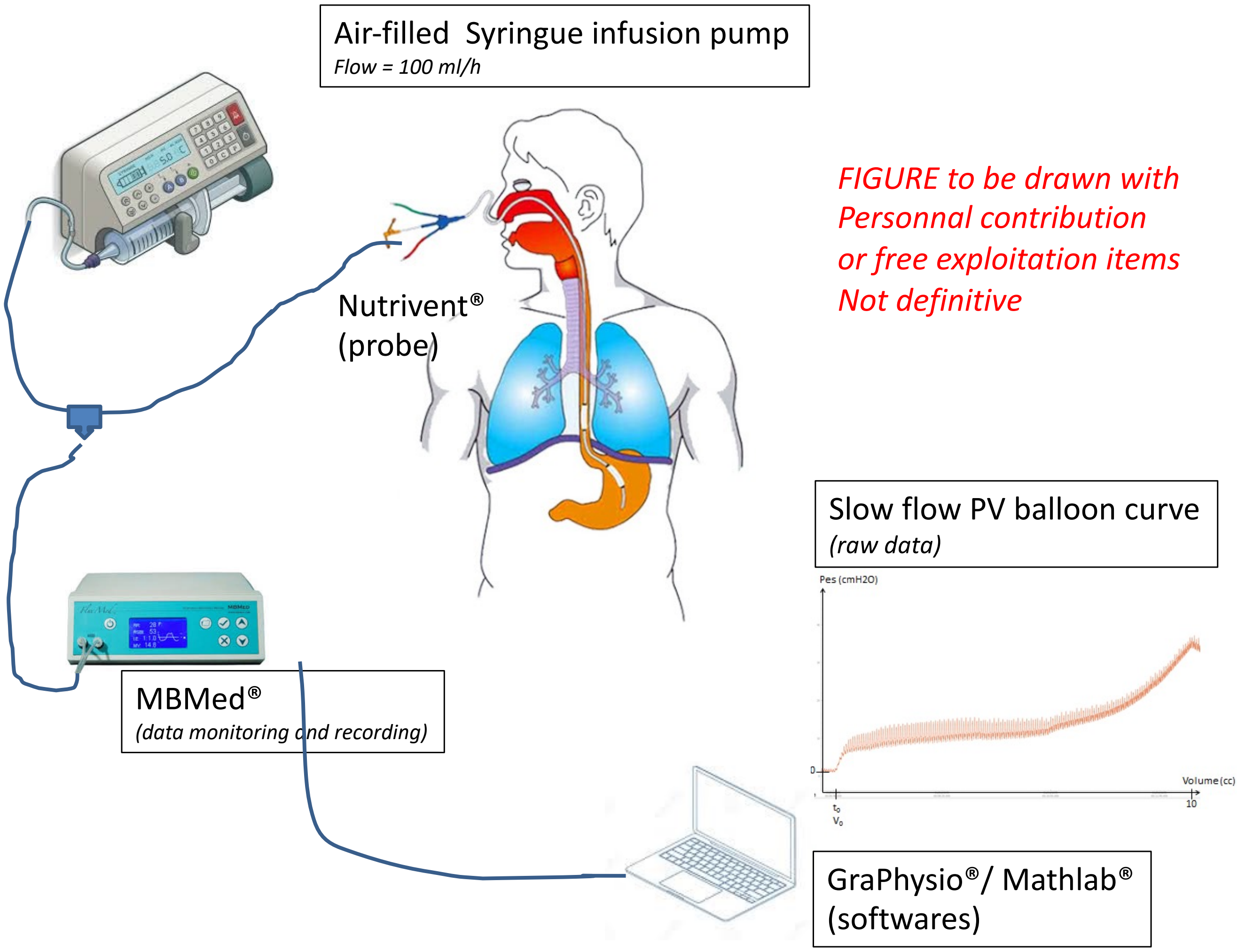
(8)Implementing a bedside assessment of respiratory mechanics in patients with acute respiratory distress syndrome . Lu Chen1,2, Guang-Qiang Chen1,2,3, Kevin Shore1, Orest Shklar4, Concetta Martins4, Brian Devenyi4, Paul Lindsay4, Heather McPhail4, Ashley Lanys2, Ibrahim Soliman1, Mazin Tuma1, Michael Kim1, Kerri Porretta4, Pamela Greco4, Hilary Every4, Chris Hayes1,2, Andrew Baker1,2, Jan O. Friedrich1,2 and Laurent Brochard1,2* Critical Care (2017) 21:84

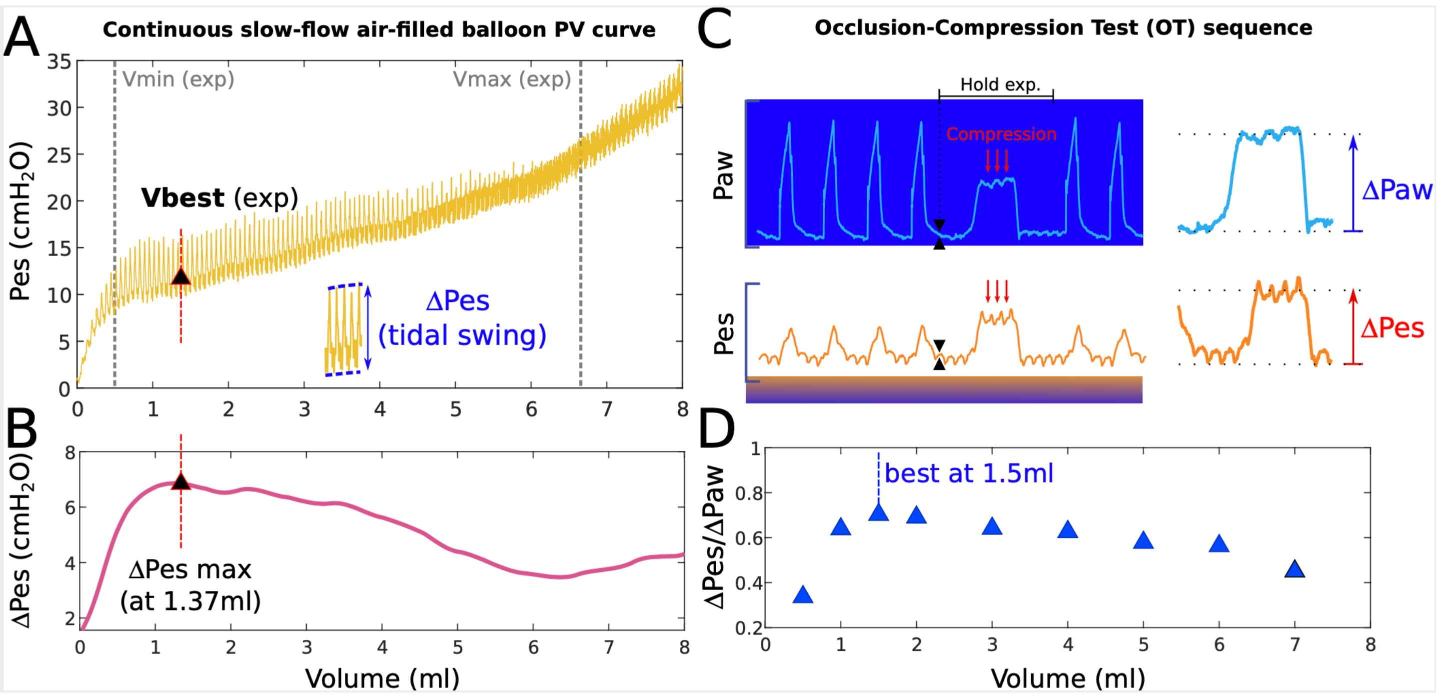
FIG&TAB (n=3)

FIG1: Experimental protocol (prototype, proprietary figure is in progress)

FIG2: Schematic record and analysis procedure of Air-filled balloon PV curve built with a slow flow inflation sequence (and subsequent occlusion test manoeuver).

TAB: (preliminary) Results form experimental PV curve (balloon volume, Peso) in subset and analysis of OT ratio for step by step calibration as described in larger population (6)


Air-filled Syringue infusion pump
Flow = 100 ml/h
Nutrivent®
(probe)
FIGURE to be drawn with
Personnal contribution
or free exploitation items
Not definitive
Slow flow PV balloon curve
(raw data)
Pes (cmH2O)
Volume (cc)
MBMed®
(data monitoring and recording)
GraPhysio®/ Mathlab®
(softwares)


A
Continuous slow-flow air-filled balloon PV curve
Vmin (exp)
Vmax (exp)
Vbest (exp)
ΔPes
(tidal swing)
Pes (cmH2O)
B
ΔPes (cmH2O)
ΔPes max
(at 1.37ml)
Volume (ml)
C
Occlusion-Compression Test (OT) sequence
Hold exp.
Compression
Paw
Pes
ΔPaw
ΔPes
D
best at 1.5ml
ΔPes/ΔPaw
Volume (ml)

	VbestXP			**VminXP**			**V4 (ml)**		**EewXP**		***OT (acceptable)***	
	Volume*	Pes(exp) §	Pes(insp)§	Volume*	Pes(exp)§	Pes(insp)§	Pes(exp)§	Pes(insp)§	Eew (slope)§§	*Pes(insp) Eew-based§*	Volume range (mean)*	varPes(exp) (range) §
P1	7.8	**20.6**	24.8	0.8	**7.2**	9.9	10.9	14.8	1.03	**11.4**		
P2	1.0	**13.4**	24.6	0.4	**12.4**	20.8	21.3	29.6	0.96	**23.6**		
P3	1.5	**9.5**	14.0	0.4	**8.1**	11.6	11.4	15.8	0.96	**12.6**		
P4	1.2	**10.9**	19.4	0.8	**9.0**	17.4	14.3	22.7	4.0	**17.5**		
P5	2.0	**15.3**	23.5	0.5	**12.4**	18.2	19.3	27.9	1.60	**20.2**		
Whole pop (n= 15)											2.8 ml	3.4 cmH2O

Legend :

P1: patient n° 1, Pn :Patient n

OT (acceptable) : volume steps where OT was within range (0.8-1.2) as recommended.

Pes(insp)Eew-based : new definition to limit esophageal wall recoil impact on Peso value: proposed as : Pes(exp) at Vmin with + [Pes(insp)-Pes(exp) at Vbest] (note that we suggest that expiratory values Peso at Vmin may be good approximation of local pleural pressure value)

*:unit= ml; §: unit = cmH2O; §§: unit = cmH2O/ml