

海外招請講演

[IL(E)20] 海外招請講演20

座長:佐藤 直樹(日本医科大学武蔵小杉病院内科・循環器内科・集中治療室)

Sun. Mar 3, 2019 8:45 AM - 9:35 AM 第5会場 (国立京都国際会館1F Room D)

[IL(E)20] Congestion in acute heart failure

Alexandre Mebazaa (University Hospitals Saint-Louis & Lariboisière, University of Paris, France)

【同時通訳付き】

University positions

2000-now Professor in Anesthesiology and Critical Care Medicine, Paris Diderot School of Medicine,
2009- now Co-Director of the Biomarker in cardiac failure team at U 942 Inserm, 42 Boulevard de la
Chapelle, 75010, Paris, France

Clinical activities

2012- now Chairman of the Department of Anesthesia and Critical Care, Hôpitaux Universitaires Saint-Louis
& Lariboisière Hospitals, 2 Rue A Paré, 75475 Paris Cedex 10, Paris, France

Major publications of the last years among 300+ articles on PubMed

Maack C, Eschenhagen T, Hamdani N, Heinzl FR, Lyon AR, Manstein DJ, Metzger J, Papp Z, Tocchetti CG, Yilmaz MB, Anker SD, Balligand JL, Bauersachs J, Brutsaert D, Carrier L, Chlopicki S, Cleland JG, de Boer RA, Dietl A, Fischmeister R, Harjola VP, Heymans S, Hilfiker-Kleiner D, Holzmeister J, de Keulenaer G, Limongelli G, Linke WA, Lund LH, Masip J, Metra M, Mueller C, Pieske B, Ponikowski P, Ristic A, Ruschitzka F, Seferovic PM, Skouri H, Zimmermann WH, Mebazaa A. Treatments targeting inotropy. *Eur Heart J.* 2018 in press
Mebazaa A, Combes A, van Diepen S, Hollinger A, Katz JN, Landoni G, Hajjar LA, Lassus J, Lebreton G, Montalescot G, Park JJ, Price S, Sionis A, Yannopoulos D, Harjola VP, Levy B, Thiele H. Management of cardiogenic shock complicating myocardial infarction. *Intensive Care Med.* 2018 in press
Léopold V, Gayat E, Pirracchio R, Spinar J, Parenica J, Tarvasmäki T, Lassus J, Harjola VP, Champion S, Zannad F, Valente S, Urban P, Chua HR, Bellomo R, Popovic B, Ouweneel DM, Henriques JPS, Simonis G, Lévy B, Kimmoun A, Gaudard P, Basir MB, Markota A, Adler C, Reuter H, Mebazaa A, Chouihed T. Epinephrine and short-term survival in cardiogenic shock: an individual data meta-analysis of 2583 patients. *Intensive Care Med.* 2018;44:847-856

Milton Packer, Christopher O' Connor, John J.V. McMurray, Janet Wittes, William T Abraham, Stefan Anker, Kenneth Dickstein, Gerasimos Filippatos, Richard Holcomb, Henry Krum, Aldo P. Maggioni, Alexandre Mebazaa, Frank Peacock, Mark C. Petrie, Piotr Ponikowski, Frank Ruschitzka, Dirk J. van Veldhuisen, Lisa S. Kowarski, Mark Schactman, and Johannes Holzmeister, on behalf of the TRUE-AHF Investigators and Committees Effect of Ularitide on Cardiovascular. Mortality in Acute Heart Failure. *N Engl J Med.* 2017, 376:1956-1964

Mebazaa A et al Recommendations on pre-hospital and early hospital management of acute heart failure: a consensus paper from the Heart Failure Association of the European Society of Cardiology, the European Society of Emergency Medicine and the Society of Academic Emergency Medicine. *Eur Heart J.* 2015;36:1958-66.

Morelli A, Ertmer C, Westphal M, Rehberg S, Kampmeier T, Ligges S, Orecchioni A, D'Egidio A, D'Ippoliti F,

Raffone C, Venditti M, Guarracino F, Girardis M, Tritapepe L, Pietropaoli P, Mebazaa A, Singer M Effect of heart rate control with esmolol on hemodynamic and clinical outcomes in patients with septic shock: a randomized clinical trial. JAMA. 2013;310:1683-91

Cohen AT, Spiro TE, Büller HR, Haskell L, Hu D, Hull R, Mebazaa A, Merli G, Schellong S, Spyropoulos AC, Tapson V; MAGELLAN Investigators. Rivaroxaban for thromboprophylaxis in acutely ill medical patients. N Engl J Med. 2013;368:513-23.

Active participation with the industry

Chairman or member of the Steering Committee of more than 15 phase II and III studies on heart failure. The most recent are: FROG-ICU (2015, data presented as Late Bracking Trial at the European Society of Intensive Care Medicine, 2015), TRUE-AHF (2016, data presented as Late Bracking Trial, in Rome at the European Society of Cardiology in August 2016).

Member of the Board or Senior Consultant of the following Medical and biotech companies:

- Sphingotec (sphingotec.com): I lead the program of assessing the prognostic value of plasma adrenomedullin in intensive care units; data are provided by the international FROG-ICU study (2200 patients). In addition, Adrenoss (600 septic shock patients, 1.5 Millions Euros) was finished in July 2016.
- Adrenomed (adrenomed.com): Chair of the Adrecizumab Program in humans (5 Millions Euros) with the objective of assessing benefits of antibodies against adrenomedulline in improving organ dysfunction in sepsis; a paper was published to recommend how to design phase II in sepsis Mebazaa A et al. Designing phase 3 sepsis trials: application of learned experiences from critical care trials in acute heart failure. J Intensive Care. 2016 31;4:24
- Magnisense: cardiovascular biomarker measured by microbeads, I helped raising 2 Millions Euros financed by BPI (Banque Publique d' Investissement, Paris France)
- Epygon (epYGON.com): minimally invasive mitral valve, member of the Board
- NeuroTronik Limited: assessing benefits of stimulations of vessels in heart failure, senior consultant

Co-owner of the following patents

- Post-partum hemorrhage score based on biomarkers (United States Patent Application 20130190585, French and World patent), licenced by Magnisense
- Calcium sensitizers for treating symptoms of venomous bites and stings Brevet (WO 2005/102347 A1)
- Biomarkers to diagnose Peripartum heart failure (Feb 2014)
- Non-invasive diagnosis of heart failure in ICU, 2 patents 2016.

For years, clinicians thought that AHF and its associated organ injury were due to reduced cardiac output. Several studies including a meta-regression of AHF trials using pulmonary artery catheter showed that cardiac output was rather preserved. When invasive hemodynamic was measured within few hours of admission for AHF in patients with acute dyspnea and with known low left ventricular ejection fraction, filling pressures of right and left ventricles were strikingly elevated. This confirms that acute pulmonary edema is related to striking increase in left atrial pressure. Increased filling pressure of the right ventricle demonstrated that patients with low left ventricular ejection fraction have also a striking congestion upstream the right ventricle. Despite striking biventricular congestion, cardiac output was preserved. In summary, congestion is the predominant clinical profile in most patients admitted with acute heart failure (AHF) and also the main mechanism of organ injury and impairment in those patients.

In AHF, injury and dysfunction of target organs such as heart, lungs, kidneys and/or liver are associated with increased risk for death. In recent years, it appeared that restoring organ function after decongestive

therapies has been associated with a lower risk for post-discharge mortality. Treatment strategies that specifically prevent, reduce or reverse organ dysfunction remain to be identified and evaluated. Defining adequate endpoints of decongestion is a major clinical challenge in AHF. Change in body weight is often used as a guide, but this approach is frequently inadequate as body weight is not increased in all patients and does not reflect congestion caused by vascular-type fluid redistribution. Novel biomarkers to achieve decongestion are needed. We recently identified the endothelial marker CD146 that is released by vascular stretch. Circulating CD146 was correlated in several cohorts to the size of inferior vena cava. Furthermore, in dialysed patients, changes in volemia between dialysis were correlated to changes in circulating CD146.

The treatment of congestion, especially acute pulmonary oedema remains largely opinion-based as there is a general lack of robust evidence to guide therapy. Yet, managing patients with AHF remains a clinical challenge and current therapies have uncertain impacts on long-term morbidity and mortality. The use of therapies that prevent or reverse congestion-induced organ injury may represent a strategy to reduce subsequent organ impairment and morbidity that is more successful than the traditional approach of targeting dyspnoea relief.