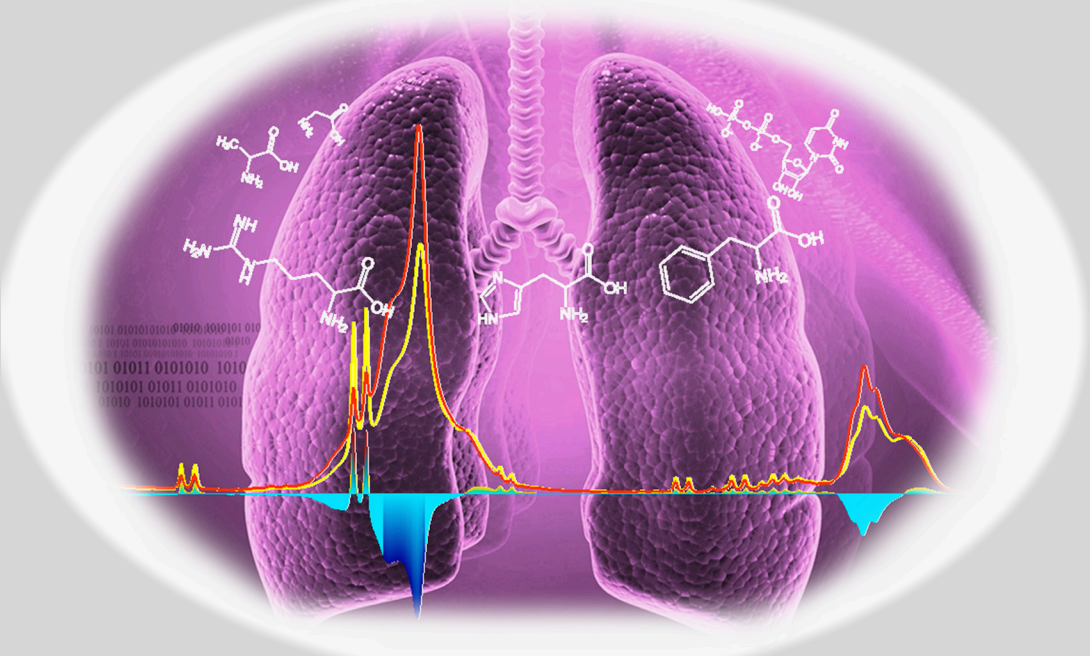
AALBORG UNIVERSITY HOSPITAL

AALBORG UNIVERSITY
DENMARK

Predictive biomarkers for the early identification of patients at risk of developing hypoxemia and acute lung injury



Clinical need

Acute Lung Injury (ALI) and/or Acute Respiratory Distress Syndrome (ARDS) are devastating, life-threatening conditions with long-term recovery associated with high morbidity and mortality (up to 40%). Worldwide, it is estimated that more than one million people are affected by ALI/ARDS every year, placing a major economic burden on society. The injury is rarely present at the time of hospital admission but develop within a week after an insult (e.g. cardiopulmonary bypass surgery, injurious ventilation, pneumonia, aspiration, sepsis, severe trauma, etc.). Preventing ALI/ARDS is a desirable goal. However, no biomarkers or diagnostic tests exist. Regarding treatment options, most of the initiated treatments failed to reverse the condition. This is probably mainly caused by the lack of predictive biomarkers to be used in monitoring the effect of initiated treatments.

Therapeutic sector

The acute lung tissue injury affects the gas exchange and primarily the oxygen uptake. The severity of ALI/ARDS is based on the degree of hypoxaemia. Hypoxaemia can be fatal, affecting all vital organs (lungs, heart, liver, kidney, brain). Hypoxemia can be improved by oxygen administration and/or through mechanical ventilation therapies. We have successfully identified several metabolites that determine the risk of developing postoperative refractory hypoxaemia and thus ALI/ARDS, providing a blood sample collected during cardiac surgery or within 40 hours postoperatively. We found that metabo-ltyping patients' journey provide new insight to the pathophysiology of acute lung injury. Our method and biomarkers have proven great potentials in early diagnosis as well as monitoring the disease development and progression into severe disease stages during and short after cardiac surgery. Hereby, this approach allows for diagnosis 2-3 days earlier than standard clinical diagnostic tests detect the ALI.

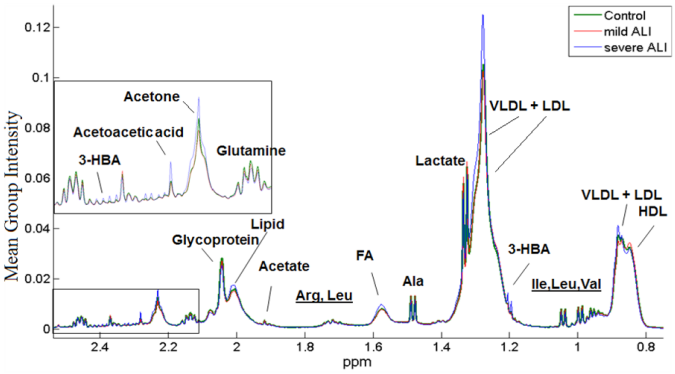


Illustration. Comparison of blood metabolic profiles of patients not developing Acute Lung Injury (ALI) ('Control'; green), patients developing 'mild ALI' (red), and patients developing 'severe ALI' (blue): Distinct metabolic changes are detected already after end surgery, allowing for early diagnosis of the disease.

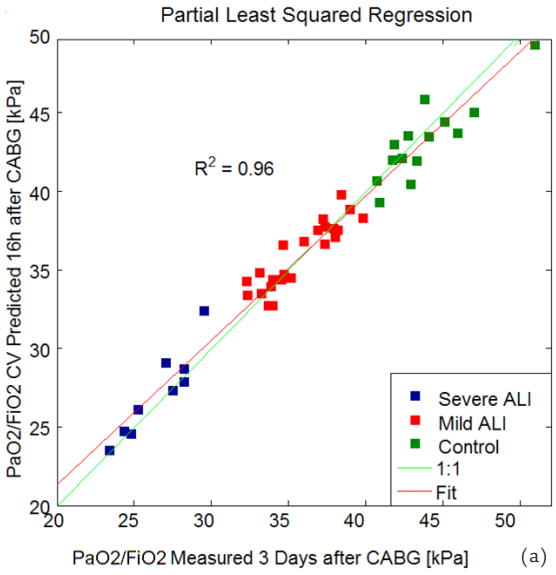
PARTNERSHIP

We are looking for:

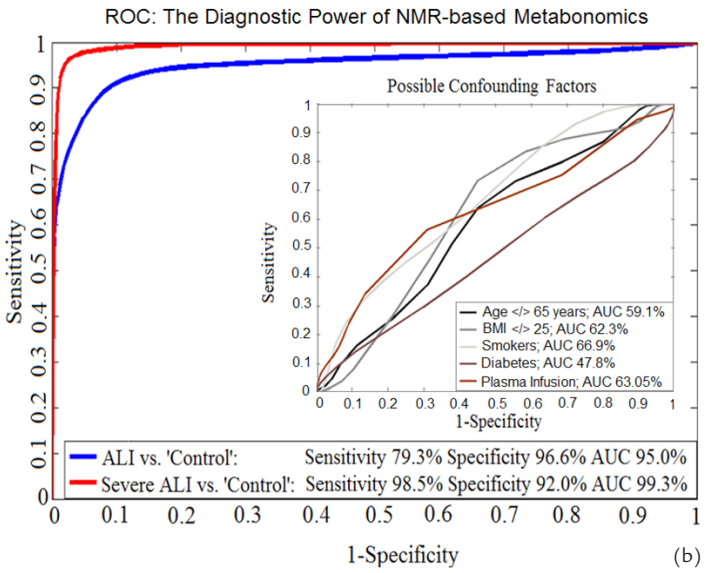
(1) develop metabolite kits to identify patients at-risk of developing refractory hypoxaemia and ALI/ARDS;
(2) develop early treatment options based on perturbed pathways.

AALBORG UNIVERSITY HOSPITAL

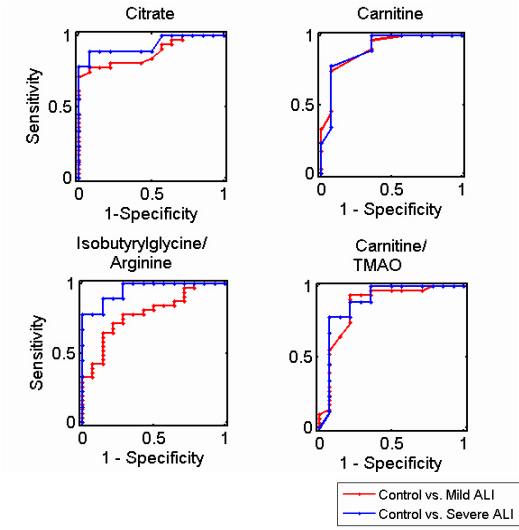
AALBORG UNIVERSITY
DENMARK



(a)



(b)



(c)

Competitive advantages

This approach could easily be implemented in current clinical practices and holds a major clinical potential by enabling early diagnosis, monitoring and treatment of postoperative complications. The economic potential is correspondingly high as the injury affects broadly, e.g. all patients mechanical ventilated have ALI/ARDS, and it is critical with hospitalization at the intensive care units (ICUs) and it has a long recovery time. Incorporating our approach into existing routine blood testing enable clinicians to screen for blood metabolic changes at a very early state and to monitor progression/regression of ALI/ARDS. Because several metabolic pathways are affected in at-risk patients, the technology may also support development of preventive treatment options.

Current Stage of technology

After the identification of the 11 biomarkers, we are currently validating the data in a second clinical trial by having access to extended blood samples. There are several commercial kits being able to measure those biomarkers individually, however, the interaction of the biomarkers are very complex. Therefore combining the specific identified biomarkers in one kit and including our algorithm analysis of the interactions will provide the clinicians with information of progression or regression of the disease. The respond time is expected within 2 hours. We are currently seeking a partnership in order to perform studies in patients developing ALI/ARDS based on other causes such as sepsis, aspiration, pneumonia and major trauma.

IP rights / patent

"Biomarkers for prediction of development of hypoxaemia due to acute lung injury" EP15168879.3. Filed on May 22, 2015.

Illustration. Metabolome screening reveals early signs of disease: (a) Partial-least Square (PLS) regression analysis reveals strong association (R2= 0.96) between early metabolic profiles and later PaO2. (b) The receiver operating characteristic (ROC) shows models' sensitivity, specificity, and accuracy. The possible influencing factors reveal no interference with the results (AUC<0.67). For validation purpouse, Monte–Carlo validation (Cal.70%, Val.30%, 5000 iterations) and permutation testing (500x) were used. No model was found over-fitted (p<0.0001). (c) Examples of ROC curve of biomarkers for the early progression into ALI after cardiac surgery.

Abbreviation: BMI= body mass index; AUC= area under the curve; Cal.= calibration; Val.= validation.

INVENTORS

Inventors: Raluca Georgiana Maltesen, Bodil Steen Rasmussen, Reinhard Wimmer, Shona Pedersen, Søren Risom Kristensen and Munsoor Ali Hanifa.

CONTACT INFORMATION

Valérie Daussin, Business Developer,
Aalborg University Hospital,
Science and Innovation Center,
Email: vkd@rn.dk, Tel: +45 97 66 62 97