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BIOMARKER RESEARCH

CBmed GmbH
Center for Biomarker Research in Medicine
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Biomarkers for Clinical Decision Support in Intensive Care

Lucas Pflanzl-Knizacek[1,2], Katharina Bergmoser[1,3], Gernot Schilcher[2], Martin Ellmerer[4], Melanie Ballach[1,2], Karin Mattersdorfer[1,2], Matthias Hafner[1,2], Lukas Pein[1,2], Philipp Eller[2], Sonja Fruhwald[2], Harald Sourij[1,2]
[1]CBmed GmbH, [2]Medical University of Graz, [3]Graz University of Technology, [4]B. Braun Melsungen AG

In intensive care, fluid balance may serve as a biomarker for critical illness. Together with the Medical University of Graz and B. Braun Melsungen AG, an in-silico model of a patients' fluid balance within the intensive care stay was developed. The model is capable of describing the patients' behaviour on fluid management in time, but also provide a prediction throughout the stay at the intensive care unit. A patent application was filed in 2018 preparing the model for translation into industrial exploitation.

Introduction and aims

In critical care as well as in many other health care disciplines, initiation of therapy is still the result of a lengthy process starting with the assessment of diagnostic biomarkers, expert decision on therapeutic measures and finally initiation of therapy or treatment. For some parameters, this process may take hours, sometimes even days. In general, it is a time consuming and workload intensive process, valuable, but lost time with regard to the disease process and from the patient perspective.

This project aimed at identifying biomarkers for relevant medical conditions in the intensive care unit, developing an algorithm for clinical decision support and implementing into a platform

Fluid balance as a biomarker for critically ill

After admission to the intensive care unit (ICU), critically ill patients receive fluids, including intravenous infusions, oral intakes or bolus injections of drugs. At the same time, losses are recorded, including urinary output, drains fluid removal by renal replacement therapy, insensible losses and others. By subtracting all losses from all intakes, one can calculate and obtain the cumulative fluid balance. A typical clinical course throughout the ICU stay is depicted in figure 1.

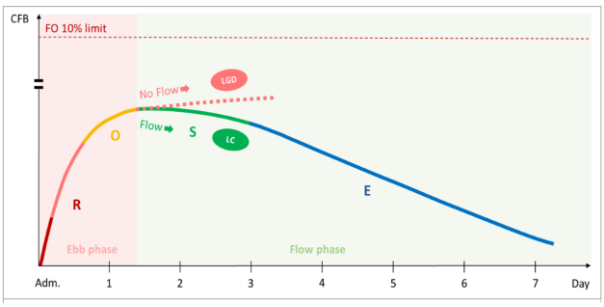

Figure 1: Clinical course of the cumulative fluid balance of a single patient. Adm...Admission to ICU, CFB...Cumulative Fluid Balance, R...Resuscitation, O...Optimization, S...Stabilization, E...Evacuation, FO...Fluid Overload, LC...Late Conservative Fluid Therapy, LGD…Late Goal-Directed Therapy. © CBmed

bmwfw Federal Ministry of Science, Research and Economy
bmvit Austrian Ministry for Transport, Innovation and Technology

The assessment of the cumulative fluid balance is regarded as a potential biomarker of critical illness due to the pathophysiological effects of fluid overload, moreover as a determinant of clinical outcome.

Model development

Within the project, the prospective clinical trial Clinibil was launched in 2016, aiming to investigate fluid and electrolyte balancing in critically ill patients undergoing elective cardiac surgery. Additionally, the retrospective study Fluidatex was set up, comprising data sets of over 2.000 patients.

Based on these two studies, methods from control systems theory were applied on patient data related to fluid management and the cumulative fluid balance.

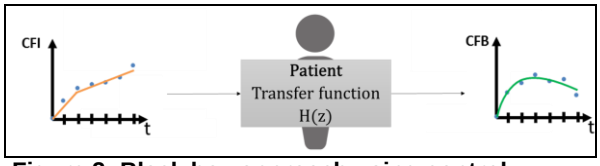

Figure 2: Black box approach using control system theory for modeling a patients' behavior on the cumulative fluid balance. CFI...Cumulative Fluid Intake, CFB...Cumulative Fluid Balance, t...time

The methodological approach is displayed in figure 2. By using the clinical available data on fluid management, a transfer function is computed for each patient using the cumulative fluid intake and the cumulative fluid balance ("black box approach"). The function enables describing a patients' specific behaviour on fluid management at a distinct point in time.

By combining the transfer function with statistical methods, i.e. linear or non-linear regressions and interpolation, we were able to develop a prediction model of the clinical course of the cumulative fluid balance.

Impact and effects

An invention was reported to CBmed and B. Braun Melsungen AG filed a patent application by December 2018.

The developed model may serve as a novel tool for intensivists to identify, compare and adjust fluid management and enable timely measures regarding specific treatments. The clinical impact of the developed model will be evaluated in the near future.

Within the duration of the project, an interdisciplinary and multi-professional project team, bridging scientists, clinical experts, intensivists and engineers has been set up and working together successfully. Several junior scientists were offered the possibility to develop their specific skill set.

The application of in-silico modelling of biomarkers may not only be limited to fluid management or intensive care. The established expertise and knowledge may be used further for new research questions in future projects.

The cooperation in this project between CBmed as a K1-Centre, the Medical University of Graz as a scientific partner and B. Braun Melsungen AG as company partner, shows how the framework of the COMET programme can be used effectively for sustainable research at the brink to translating findings towards industrial exploitation.

Contact and information
K1-Centre CBmed GmbH

CBmed GmbH
Stiftingtalstrasse 5, 8010, Graz
T +43 316 385 28801
E office@cbmed.at, www.cbmed.at

Project coordinator
Dipl.-Ing. Lucas Pflanzl-Knizacek, BSc, MA

Project partners

Organisation	Country
B.Braun Melsungen AG, Entwicklungsbüro Graz	Austria
Medical University of Graz	Austria