

ISICEM15: Personalised Medicine in Critical Care - the Future?



Is personalised medicine the future for critical care? Hector R. Wong (Cincinnati, USA), speaking at the 35th International Symposium on Critical Care and Emergency Medicine in Brussels last month, suggested it is, given that intensivists generally manage heterogeneous syndromes, such as ARDS, AKI and sepsis, rather than distinct diseases. In critical care this would entail diagnostic testing to define subclasses of “endotypes” of critical illness syndromes and customised therapy based on these endotypes. Critical illness and decision-making is time-sensitive, and any personalised medicine approach in critical care must meet the time-sensitive demands of the critically ill patient, he emphasised.

Wong gave the example of enrolment in sepsis critical care trials today. When sepsis is defined by clinical criteria, patients are included or excluded according to clinical criteria and mortality risk may be taken into account with APACHE score. Sepsis clinical trials in the personalised medicine future would perhaps enrol patients with sepsis defined by molecular and biological criteria, with more accurate estimation of baseline mortality risk, so that trials can evaluate who stands to actually benefit from an experimental therapy and assess the actual biology to determine what the sepsis endotype is and how it affects the response to the experimental therapy. Ideally that would lead to enrolling and randomising a more homogeneous cohort of patients with a greater likelihood of benefit.

Transcriptomics is a decade-long effort that centres on genome-wide expression profiling, resulting in a multi-institutional biological and clinical repository. The hope is to discover candidate diagnostic biomarkers, candidate stratification biomarkers and sepsis subclasses. This will assist in answering the question “What is my patient’s biological response to sepsis and how may that information inform my clinical decision making?”

[Wong and colleagues](#) identified and validated a gene expression-based subclassification strategy for paediatric septic shock in their research published in BMC Medicine in 2009 and [Critical Care Medicine](#) in 2011. In their post-hoc phenotype analysis of expression-based subclasses, they found that subclass A patients had [significantly higher illness severity, rates of organ failure and mortality \(36% vs 11%\)](#). They have evaluated 300 patients with this approach, reduced the subclass-defining gene signature to the top 100 class-predictor genes and aim to develop a clinical test that can be used in critical care. The genes that enable sub classification correspond to adaptive immunity and the glucocorticoid receptor signalling pathway. They also found that the use of corticosteroids is independently associated with four times the risk of dying in the subclass A patients.

Concluded Wong, personalised medicine is the future for critical care, because we mostly deal with heterogeneous syndromes, which are potentially more manageable via personalised medicine concepts. But it will need widespread collaboration and resources. Translating research to the bedside is the next challenge.

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