The relationship between the use of loop diuretics, congestion and heart failure outcome

CHAPTER 11

VALORISATION

During the past four years I focused my clinical and research interest on the excellence of diagnostics and management of acute and chronic heart failure. In particular, I analysed in depth the interactions between congestion, its management with diuretics, and the effects of (de)congestion on heart failure outcome. My research interest was driven by the current gaps in knowledge about an optimal decongestive approach and the absence of a reliable biomarker assisting in congestion detection and grading. I tried to fill some of these gaps by analysing the interactions between congestion, its treatment, and heart failure outcome as well as by searching for novel tools for congestion detection and grading. My research resulted in several key findings, that altogether make a relevant background for optimised clinical practice and future research.

Firstly, my research revealed that in daily clinical practice clinicians should not rely on a single clinical parameter when screening patients for the presence of congestion. In fact, I was able to demonstrate that heart failure patients may present with different phenotypes of congestion. This finding underscores the importance of systematic clinical evaluation, which is rarely done in daily clinical practice. In order to facilitate congestion detection and grading I came up with an easily applicable clinical congestion index, consisting of 7 clinical markers of water retention in the human body. My research reveals that this novel clinical toll is highly predictive of morbidity and mortality. Clinical congestion index does not require neither expensive laboratory testing, nor any highly specific knowledge / skills. This makes it a simple tool for daily clinical evaluation.

Secondly, the more congested the patients were, the worse was the survival and heart failure hospitalisation-free survival. This finding underscores the importance of screening heart failure patients for congestion, which is not always the case. I believe that the publication of these results increased the awareness of congestion detection, even in apparently stable chronic heart failure patients.

Thirdly, the uncertainties about the safety of (high dose) loop diuretic treatment often result in suboptimal treatment and persistent congestion. To some extent, there exists some level of congestion tolerance in a real-world setting, as reflected by the findings from heart failure registries as well as by the high prevalence of congestion in TIME-CHF patients at baseline. However, my research does not justify this approach by revealing that high dose loop diuretic management / thiazide co-administration does not independently predict worse outcome. In fact, treatment intensification that does not result in clinical decongestion leads to the worst outcome. This finding is very important from a practical point of view. In particular, the present findings shift the contemporary congestion management paradigm from ‘lower dose is better’

to ‘effective dose is the best’. This means that in daily practice clinicians should try to decongest heart failure patients, even if high dose of a loop diuretic or a co-administration of a thiazide is needed.

Fourthly, clinical congestion is already a late manifestation of fluid accumulation in a human body. Therefore, the future aim should be to detect congestion non-invasively before clinical signs and symptoms become apparent. I was able to demonstrate that bio-ADM and sCD146 are both capable to reflect congestion as assessed by means of clinical evaluation and sonographic assessment. This finding creates a relevant background for future interventional trials, assessing the role of bio-ADM and/or sCD146 in decongestion guidance.

To sum up, my research adds significantly to the understanding of the complex interactions between congestion, its treatment with diuretics, and heart failure outcome. I was able to come up with three novel biomarkers of congestion detection and grading, i.e. clinical congestion index, bio-ADM, and sCD146. They all showed to reflect the presence and the degree of congestion, which should not be tolerated in clinical practice.