

The Trial of Intensified Medical Therapy in Elderly patients with Congestive Heart Failure (TIME-CHF)

Citation for published version (APA):

Maeder, M. T. (2018). *The Trial of Intensified Medical Therapy in Elderly patients with Congestive Heart Failure (TIME-CHF): novel insights into hot topics in heart failure*. Datawyse / Universitaire Pers Maastricht. <https://doi.org/10.26481/dis.20180614mm>

Document status and date:

Published: 01/01/2018

DOI:

[10.26481/dis.20180614mm](https://doi.org/10.26481/dis.20180614mm)

Document Version:

Publisher's PDF, also known as Version of record

Please check the document version of this publication:

- A submitted manuscript is the version of the article upon submission and before peer-review. There can be important differences between the submitted version and the official published version of record. People interested in the research are advised to contact the author for the final version of the publication, or visit the DOI to the publisher's website.
- The final author version and the galley proof are versions of the publication after peer review.
- The final published version features the final layout of the paper including the volume, issue and page numbers.

[Link to publication](#)

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal.

If the publication is distributed under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license above, please follow below link for the End User Agreement:

www.umlib.nl/taverne-license

Take down policy

If you believe that this document breaches copyright please contact us at:

repository@maastrichtuniversity.nl

providing details and we will investigate your claim.

Chapter XII

Valorisation

The present work is a summary of pre-specified analyses and post-hoc studies of the largest study on natriuretic peptide-guided therapy in oldest and most comorbid heart failure population. None of the studies has provided definite results on a particular topic but we think that some results have extended existing concepts and others form the basis for pathophysiological considerations and future studies. Thus, we think that the present work represents a valuable contribution to the literature.

The findings on worsening renal function (WRF) are important as they provide reassurance that the recently developed concept of “pseudo-WRF” is relevant not only for the acute heart failure setting but also the chronic setting. The results have direct implications for clinical practice in that doctors do not have to worry too much about changes in serum creatinine in heart failure patients as long as patients do clinically well during the up-titration of neurohormonal blockade, and that reduction of heart failure therapy is not required in this setting. On the other hand the findings underscore the notion that a therapy mainly consisting of high loop diuretic doses represents a marker and maybe also a mediator of a poor prognosis, and maximal efforts are required to maximize neurohormonal blockade and minimize loop diuretic doses. The data also highlight the importance of close monitoring of serum creatinine and potassium, in particular in elderly and comorbid patients.

The findings on heart rate are novel in that they clearly show that the prognostic impact of heart rate depends on age, a finding which did not well emerge from the SHIFT data because this study did not include many older patients. This has clinical implications with regards to the practice of the up-titration of betablockers and the use of ivabradine in elderly patients. Both classes of drugs are recommended in guidelines based on studies in relatively young patients, but the optimal heart rate in sinus rhythm in elderly patients will have to be defined in future studies. In addition, we have shown that we will have to think about the heart rate target in patients with heart failure and atrial fibrillation and the best way we should achieve this. This is largely unknown, and our and other studies have indicated a need for further research in this area. Although a simple parameter, our findings on delta heart rate are novel and promising. It would be very attractive if a simple bedside test could help to refine the prognostic assessment in a significant manner. However, further studies with delta heart rate measured in a more standardized fashion and exploring its pathophysiological correlates as well as the confirmation of the prognostic data in other cohorts are required.

The concept of natriuretic peptide-guided heart failure therapy has been evaluated in several studies, and findings are consistent in that younger patients with HFrEF derive benefit. We were the first to show that the intervention of natriuretic peptide-guided therapy has a sustained prognostic impact even after termination of NT-proBNP-guided up-titration of therapy. Second, we have shown that the concept of natriuretic peptide-guided therapy seems not to work in patients with HFpEF in whom left ventricular structure and function clearly differs from that in HFrEF. Thus, TIME-CHF including the present analyses has provided an important contribution to define the application of natri-

uretic peptide-guided therapy in heart failure. On the other hand, TIME-CHF has revealed that future research must address the question how to tailor heart failure therapy in elderly patients in general, and particular in those with HFpEF for whom there is still no drug with established prognostic benefit.