

# Markers of hypercoagulation in cardiovascular disease in the general population

Citation for published version (APA):

van Paridon, P. (2022). *Markers of hypercoagulation in cardiovascular disease in the general population*. [Doctoral Thesis, Maastricht University]. Maastricht University. <https://doi.org/10.26481/dis.20220609pp>

## Document status and date:

Published: 01/01/2022

## DOI:

[10.26481/dis.20220609pp](https://doi.org/10.26481/dis.20220609pp)

## Document Version:

Publisher's PDF, also known as Version of record

## Please check the document version of this publication:

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## Chapter 7: Impact paragraph

Despite global efforts, CVD is still the leading cause of disease and disability worldwide. Even though efforts to control traditional CVRFs have been effective, the rising numbers are concerning, predominantly in the developing countries.<sup>1</sup> By 2030 the total global cost of CVD is set to rise from approximately €713 billion (2010) to a staggering €863 billion.<sup>2,3</sup>

More than ever, there is medical and economical need for a different approach in managing prevention of CVD and a search for novel biomarkers, as a step towards personalized medicine. The TGA, a widely-used tool in thrombosis and hemostasis research, offers an estimate of the clotting potency of a given plasma sample. In a research setting, TGA is an established tool that is able to detect bleeding tendency (hypocoagulability) and venous thrombosis (hypercoagulability), while associations with arterial thrombosis are conflicting. The clinical validation of the TGA in relation to arterial and/or venous thrombosis remains to be addressed. Therefore, we researched TGA in the context of age, sex, traditional CVRFs, CVD and overall mortality (**chapter 2**) and investigated the biochemical determinants of the TGA (**chapter 3**). The analysis in **chapter 2** demonstrates that lag time (time needed for the thrombin to form) and ETP (overall amount of thrombin formed over time), two parameters of TGA, are associated with increased mortality. Due to the high prevalence of CVD in the general population, we may presume that the majority of the deaths are related to CVD. It illustrates that parameters of TGA might be valuable as a prognostic factor in the individual CVD risk assessment and deciding whether a patient needs additional anticoagulant or anti-inflammatory therapy.

At this point in time, TGA remains a relatively costly and labor-intensive test. However, its potential to develop into a bedside lab testing to address the overall coagulation “status” of a patient is feasible. The consequences of early detection of hypercoagulability to guide preventive management, in particular in high risk situations (post-operative, during pregnancy, COVID-19, cancer patients) could have impact on optimizing thrombosis prophylaxis, which would consequently improve the quality of life of patients.

A topical example: we learned from the COVID-19 epidemic that DVT or PE occurs in 21% of the hospitalized COVID-19 patients and 31% of the COVID-19 patients admitted to the intensive care unit, in spite of prophylactic doses of low-molecular-weight heparin (LMWH).<sup>4</sup> At present, we are not able to determine which COVID-19 patients are at risk for developing VTE under prophylactic LMWH. At the same time, over-prescribing or administering too high doses of LMWH to COVID-19 patients would increase bleeding risk, impacting quality of life, morbidity and mortality.<sup>5</sup> TGA could be used to detect patients at high risk, and could therefore be helpful to optimize individualized prophylactic LMWH treatment.

**Chapter 4** and **chapter 5** describe the associations of TFPI and vWF on CVD(-related death). Inexpensive biomarkers for assessing the cardiovascular

risk are of increasing interest, as they may contribute to risk stratification, ultimately aiming for more cost effective disease management.<sup>6</sup> Timely observation of endothelial cell dysfunction through TFPI measurement may be a starting point for more expeditious use of endothelial cell protective medication, like statins. For the latter, further research is required to answer the question whether statins could reduce TFPI levels and endothelial dysfunction, regardless of baseline LDL levels.

## References

1. Bowry ADK, Lewey J, Dugani SB, Choudhry NK. The Burden of Cardiovascular Disease in Low- and Middle-Income Countries: Epidemiology and Management. *Can J Cardiol.* 2015;31: 1151–1159.
2. World Health Organization. Global Atlas on Cardiovascular Disease Prevention and Control. *World Health Organization;* 2013.
3. Shaw LJ, Goyal A, Mehta C, Xie J, Phillips L, Kelkar A, et al. 10-Year Resource Utilization and Costs for Cardiovascular Care. *J Am Coll Cardiol.* 2018;71: 1078–1089.
4. Malas MB, Naazie IN, Elsayed N, Mathlouthi A, Marmor R, Clary B. Thromboembolism risk of COVID-19 is high and associated with a higher risk of mortality: A systematic review and meta-analysis. *EClinicalMedicine.* 2020;29: 100639.
5. Cohen AT, Agnelli G, Anderson FA, Arcelus JI, Bergqvist D, Brecht JG, et al. Venous thromboembolism (VTE) in Europe. The number of VTE events and associated morbidity and mortality. *Thromb Haemost.* 2007;98: 756–764.
6. Vasan Ramachandran S. Biomarkers of Cardiovascular Disease. *Circulation.* 2006;113: 2335–2362.