

***Distinctive Alterations in Microvascular Function
due to Multiple Common Morbidities***

1. Metabolic derangements, with or without CKD, induce oxidative stress and coronary microvascular dysfunction associated with left ventricular diastolic dysfunction; the latter is mediated by intrinsic cardiomyocyte stiffening with or without increased extracellular matrix deposition. (this thesis)
2. Exposure to multimorbidity results in perturbations in myocardial oxygen balance, which is not only due to reduced myocardial oxygen efficiency and a subsequent increased basal myocardial oxygen demand but also due to coronary microvascular dysfunction. (this thesis)
3. Causes and clinical consequences of microvascular dysfunction are organ specific. (this thesis)
4. Von Willebrand Factor is a suitable biomarker for advanced cardiovascular disease (this thesis).
5. Pulmonary microvascular dysfunction occurs already early in the pathogenesis of heart failure with preserved ejection fraction, i.e. well before overt left ventricular backward failure is present. (this thesis)
6. The approach of combining multiple comorbidities is the best way to model HFpEF. (O’Gallagher and Shah, Cardiovascular Research 2018)
7. Clinical classifications were introduced to simplify complex biological systems, but often single cut-off values fail to separate disease entities, especially in multifactorial diseases and in aging patient populations. (Optiz *et al.* Journal of the American College of Cardiology 2016)
8. Therapeutic studies should stratify patients with microvascular dysfunction based on impairment of resting or hyperemic flow. (Rahman *et al.* Journal of the American College of Cardiology 2020)
9. Large research funding agencies need to go further down the translation road by reforming the monopoly of ‘a single investigator’-driven research grants as their main funding mechanism. This system rewards individual success and does little to encourage the type of collaboration that translational research demands. (Butler, Nature 2008)
10. Microvascular dysfunction is the culprit for severe infections with COVID-19 (Guzik *et al.* Cardiovascular Research 2020)
11. Dubito, ergo cogito, ergo sum (ik twijfel, dus ik denk, dus ik ben) – René Descartes, *Principia philosophiae* 1644.