Study protocol for the randomized controlled TREASURE trial: timely recovery after subclinical heart failure

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Objective. Heart failure (HF) significantly impacts women, with half experiencing diastolic dysfunction and preserved ejection fraction (HFpEF). Anatomically, this is paralleled by absolute (Left Ventricular Hypertrophy (LVH)) or relative cardiac hypertrophy (concentric hypertrophy, HF stage B). Preeclampsia (PE) is accompanied with cardiac hypertrophy, with 40% remaining after delivery. Focusing on the early HF phase, pharmacological interventions, mainly angiotensin-converting enzyme (ACE) inhibitors, show promise in slowing progression towards symptomatic HF in the high-risk population of women. We propose a randomized controlled trial to assess the effectiveness of ACE inhibitors *versus* standard care) in reversing asymptomatic heart failure (HF stage B) and/or diastolic dysfunction during a two-year open-label treatment period for formerly preeclamptic women.

Materials and Methods. We will recruit women 18 years and older with asymptomatic HF and/or diastolic dysfunction, 0.5 to 30 years postpartum, from cardiovascular risk management screening at Maastricht University Medical Center+. A total of 130 women will be 1:1 randomized for perindopril or no medication. Outcome measures will include cardiac echocardiographic parameters, blood pressure, quality of life, metabolic factors, endothelial function, and novel biomarkers.

Results. The two-year study with biannual follow-ups will include advanced echocardiography, questionnaires, blood pressure measurements, and laboratory screening. Anticipated results expect substantial improvement in the perindopril group, confirmed by echocardiography with a left ventricular mass index < 95 g/m^2, relative wall thickness ≤ 0.43, left ventricular ejection fraction $\geq 55\%$, and maintained normal diastolic function.

Conclusions. This trial aims to evaluate if ACE inhibitors treatment can normalize HF stage B and/or diastolic dysfunction in formerly preeclamptic women.