



UKE Paper of the Month November 2023

High-Sensitivity Cardiac Troponin I Enhances Preeclampsia Prediction Beyond Maternal Factors and the sFlt-1/PlGF Ratio

L. Bacmeister, A. Goßling, A. Buellbach, A. Birukov, J.E. Myers, S.T. Thomas, S. Lee, M.S. Andersen, J.S. Jorgensen, A. Diemert, S.M. Blois, P.C. Arck, K. Hecher, F. Herse, S. Blankenberg, R. Dechend*, D. Westermann*, T. Zeller*

[Circulation. 2023 Nov 20;doi: 10.1161/CIRCULATIONAHA.123.066199.](https://doi.org/10.1161/CIRCULATIONAHA.123.066199)

ABSTRACT:

Background: Preeclampsia shares numerous risk factors with cardiovascular diseases. Here, we aimed to assess the potential utility of high-sensitivity cardiac troponin I (hs-cTnI) values during pregnancy in predicting preeclampsia occurrence.

Methods: This study measured hs-cTnI levels in 3,721 blood samples of 2,245 pregnant women from 4 international, prospective cohorts. Three analytical approaches were used: (1) a cross-sectional analysis of all women using a single blood sample, (2) a longitudinal analysis of hs-cTnI trajectories in women with multiple samples, and (3) analyses of prediction models incorporating hs-cTnI, maternal factors, and the sFlt-1 (soluble fms-like tyrosine kinase 1)/PlGF (placental growth factor) ratio.

Results Women with hs-cTnI levels in the upper quarter had higher odds ratios for preeclampsia occurrence compared with women with levels in the lower quarter. Associations were driven by preterm preeclampsia (odds ratio, 5.78 [95% CI, 2.73-12.26]) and remained significant when using hs-cTnI as a continuous variable adjusted for confounders. Between-trimester hs-cTnI trajectories were independent of subsequent preeclampsia occurrence. A prediction model incorporating a practical hs-cTnI level of detection cutoff (≥ 1.9 pg/mL) alongside maternal factors provided comparable performance with the sFlt-1/PlGF ratio. A comprehensive model including sFlt-1/PlGF, maternal factors, and hs-cTnI provided added value (cross-validated area under the receiver operator characteristic, 0.78 [95% CI, 0.73-0.82]) above the sFlt-1/PlGF ratio alone (cross-validated area under the receiver operator characteristic, 0.70 [95% CI, 0.65-0.76]; $P=0.027$). As assessed by likelihood ratio tests, the addition of hs-cTnI to each prediction model significantly improved the respective prediction model not incorporating hs-cTnI, particularly for preterm preeclampsia. Net reclassification improvement analyses indicated that incorporating hs-cTnI improved risk prediction predominantly by correctly reclassifying women with subsequent preeclampsia occurrence. **Conclusion:** These exploratory findings uncover a potential role for hs-cTnI as a complementary biomarker in the prediction of preeclampsia. After validation in prospective studies, hs-cTnI, alongside maternal factors, may either be considered as a substitute for angiogenic biomarkers in health care systems where they are sparse or unavailable, or as an enhancement to established prediction models using angiogenic markers

STATEMENT:

Our work opens a new view on cardiovascular biomarkers and their usability in so far unrelated diagnostic areas. Furthermore, our work represents an interdisciplinary work between obstetrics and cardiology.

BACKGROUND:

This work was performed as a collaboration of two UKE Departments, the Department of Cardiology with the groups of Tanja Zeller and Dirk Westermann (formerly UKE) and the Department of Obstetrics and Fetal Medicine (P. Arck, A. Diemert, K. Hecher). The groups around Tanja Zeller and Dirk Westermann are interested in cardiovascular biomarkers whereas the team of Obstetrics and Fetal Medicine has a research focus on the fetomaternal immune cross-talk. Jointly with their national and international colleagues the UKE groups performed this research project.