Diagnostic accuracy of different sFlt-1 and PlGF cut-off values in the assessment of preterm and term preeclampsia

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Objective
Differences in the circulating antiangiogenic factor, soluble vascular endothelial growth factor receptor-1 (sFlt-1), and the proangiogenic placental growth factor (PlGF) seem to accurately predict preeclampsia (PE). The objective of this study was to investigate diagnostic accuracy of different cut-off values in preterm (< 36+6 weeks) and term PE (> 37+0 weeks).

Methods
A prospective cohort study was performed at the University Hospital of Basel and Geneva from 1/2012 until 3/2015. Pregnant women with singleton pregnancies and high risk to develop PE or with symptoms were approached. Only blood samples on day of PE diagnosis were included and compared to a GA matched high risk control group (+/- 4 days). Primary outcome was to verify the PE diagnosis using the recently proposed cut-off values for PE prediction (sFlt-1:PlGF ratio of > 85 in < 34 weeks of gestation (WOG) or > 110 in > 35 WOG), calculated and reference GA dependent quantiles.

Results
In the preterm PE subset, 34 PE women (31+1 weeks; IQR 21+4- 36+6) were matched with 52 controls (30+3 weeks; IQR 21+2-36+5). Sensitivity and specificity of the ratio of the pre-specified cut-off values were 94% [95% confidence interval (CI) 80-99%] and 96% (95% CI, 87-100%), respectively. Similar performance was achieved by the 95th quantile of the ratio, the 95th quantile of sFlt-1 and the 5th quantile of PlGF. In the term PE subset, 23 PE women were matched with 35 controls; gestational age (38+6 weeks; IQR 37+0-41+4). Sensitivity and specificity of the pre-specified cut-off values were 30% (95% CI, 13-53%) and 97% (95% CI, 85-100%), respectively. Similar performance was achieved by the 95th quantile of the ratio, the 95th quantile of sFlt-1 and the 5th quantile of PlGF. However, the performance was improved when 90th quantile of sFlt-1 was used with sensitivity and specificity of 78% (95% CI, 56-93%) and 89% (95% CI, 73-97%), respectively. The reference GA dependent quantiles added no further benefit.

Conclusion
In a high risk population, the 90th quantile of the single biomarker sFlt-1 seems to be superior to the ratio of sFlt-1:PlGF in the assessment of PE in term pregnant women.

Figure 1. Receiver operator characteristic curve analysis for sFlt-1:PIGF ratio and single biomarkers for the detection of a) preterm PE and b) term PE.