# A High-Precision Machine Learning Approach Comparing AGT/VASN Ratio and sFlt-1/PlGF for Severe Preeclampsia Diagnosis: A Case-Control Study



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## Background

•**The Diagnostic Gap:** Preeclampsia (PE) affects 5–8% of pregnancies,  diagnostic criteria primarily detects late-stage disease.

• **Limitation:** Current soluble biomarkers (sFlt-1/PlGF) provide high negative predictive value but suffer from marginal positive predictive performance (PPV), limiting their early clinical utility.

•**Novel Mechanistic Candidates:** Preliminary research identified Angiotensinogen (AGT) and Vasorin (VASN) as biomarkers that mirror the profiles of established standards while offering a broader mechanistic view of vascular health.

•**Vessel Reactivity:** While traditional Doppler measures steady-state flow, the Vascular Reactivity Index (VRI) captures the mechanistic driver of PE—vessel reactivity—using operator-independent technology.

•**Hypothesis:** Multimodal integration of novel biochemical markers (AGT/VASN), physiological reactivity (VRI), and clinical data via ML will significantly boost diagnostic precision and overcome the PPV limitations of current models

# Design and Methods



**Study Cohort:** A well-characterized, racially balanced, and GA-matched cohort of 72 pregnant women (43 sPE; 29 NTP).

**Data Acquisition:**

**Biochemical:** Quantification of serum VASN, AGT, sFLT-1, and PlGF via standardized ELISA.

**Physiological:** Vessel reactivity measured via the Vendys II digital thermal monitoring system (VRI).

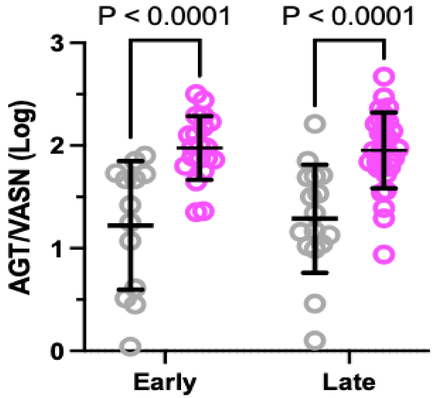
**ML Development Pipeline:**

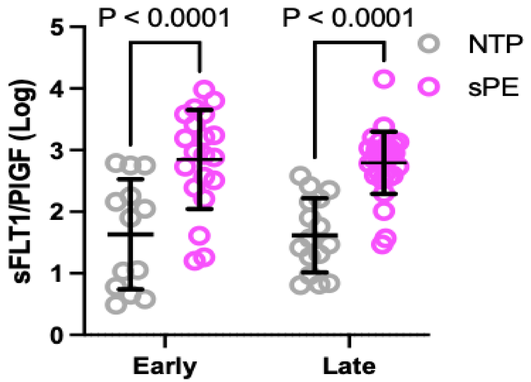
**Preprocessing:** Regularized logarithm (RLD) transformation was applied to stabilize variance across the dataset.

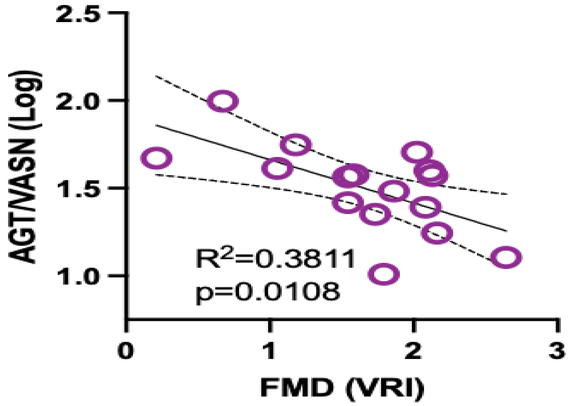
**Model Selection:** Comparison of Logistic Regression (LR), Random Forest (RF), and Support Vector Machines (SVM).

**Optimization:** Used Recursive Feature Elimination (RFE) to identify top predictors and maximize PPV.

# Results




| Model | Data | AUC | Sens | Spec | PPV | NPV | Gap | NRI | NRI CI | DeLong_p |
|---|---|---|---|---|---|---|---|---|---|---|
| AGT | Log | 0.79 | 0.6 | 0.862 | 0.434 | 0.924 | 0.002 | -0.132 | [-0.46-0.18] | 0.035 |
| VASN | Log | 0.852 | 0.84 | 0.759 | 0.38 | 0.964 | 0.003 | -0.161 | [-0.43-0.12] | 0.178 |
| sFLT-1 | Log | 0.852 | 0.76 | 0.862 | 0.493 | 0.953 | 0.003 | -0.06 | [-0.22-0.10] | 0.029 |
| PlGF | Log | 0.83 | 0.8 | 0.759 | 0.369 | 0.956 | -0.024 | -0.118 | [-0.28-0.02] | 0.009 |
| AGT/VASN | Log | 0.88 | 0.82 | 0.862 | 0.512 | 0.964 | -0.005 | -0.069 | [-0.35-0.26] | 0.382 |
| sFLT1/PlGF | Log | 0.899 | 0.82 | 0.862 | 0.512 | 0.964 | -0.004 | 0 | [0.00-0.00] | 1 |
| Combined_Score | RLD | 0.943 | 0.88 | 0.897 | 0.6 | 0.977 | -0.008 | 0.138 | [-0.07-0.35] | 0.051 |
| Random Forest (Refined) | RLD | 0.913 | 0.9 | 0.828 | 0.479 | 0.979 | 0.067 | 0.158 | [-0.05-0.34] | 0.327 |
| SVM (Refined) | RLD | 0.947 | 0.9 | 0.897 | 0.606 | 0.981 | 0.009 | 0.207 | [0.02-0.42] | 0.028 |
| Logistic Regression (Refined) | RLD | 0.949 | 0.9 | 0.897 | 0.606 | 0.981 | 0.007 | 0.227 | [0.02-0.45] | 0.033 |

# Conclusions and Discussion



- **Validation of Novel Markers:** AGT and VASN are validated as powerful mechanistic biomarkers that perform comparably to current clinical standards.
- **Solving the PPV Problem:** The primary gain of our ML-aided approach is a substantial increase in positive predictive value, addressing the main limitation of current diagnostic models.
- **Synergistic Integration:** Combining biochemical ratios with physiological reactivity (VRI) provides a higher-power diagnostic tool than individual markers alone.
- **Resistance to Adiposity:** The markers reflect underlying PE pathophysiology rather than maternal adiposity, supporting their use in diverse, high-BMI populations.
- **Technical Proof-of-Concept:** These findings establish a rigorous technical foundation for the development of multimodal algorithms for predictive obstetric care.