Machine Learning Analysis of Arterial Stiffness Trends throughout Pregnancy for Early Prediction of the Development of Preterm, Term and Postpartum Preeclampsia

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What is Preeclampsia ?

- A serious disorder of pregnancy[1]:
  Hypertension + **End-organ damage** (Kidney, Liver)
  - Devastating consequences for both the pregnant patient and baby
- Affects **5-8% of pregnancies globally**[1] and **70 000 maternal deaths** yearly
- Current management in most cases = Delivery

A knowledge gap...

Uterine Artery Doppler (UAD)

Angiogenic Factors
Ex. Placental GF and protein 13

Moderate predictive ability for term and postpartum PrE [4,5]

Classification based on **time of onset**[2,3]

Preterm
Onset prior 34 wks gestation

Term
Onset after 34 wks gestation

Post-Partum
Onset after delivery

* Term pregnancy = 40 wks

[1] Auger N, Luo ZC, Nuyt AM, et al. Secular Trends in Preeclampsia Incidence and Outcomes in a Large Canada Database: A Longitudinal Study Over 24 Years. The Canadian journal of cardiology 2016;32:987.e15-23.
[2] Phillips, J. K., Janowiak, M., Badger, G. J., & Bernstein, I. M. (2010). Evidence for distinct preterm and term phenotypes of preeclampsia. The Journal of Maternal-Fetal & Neonatal Medicine, 23(7), 622–626. https://doi.org/10.3109/14767050903258746
[3] Johnson, A., Federico, C., Martinez, M., Tran, K.-A., Kao, E., Hooshvar, N., Tice, D., Wu, G., Gambala, C., Pridjian, G., & Dola, C. (2015). [192-POS]. Term and preterm preeclampsia: Are there two distinct phenotypes? Pregnancy Hypertension: An International Journal of Women's Cardiovascular Health, 5(1), 97. https://doi.org/10.1016/j.preghy.2014.10.198
4 Henderson, J. T., Thompson, J. H., Burda, B. U., Cantor, A., Beil, T., & Whitlock, E. P. (2017). Screening for Preeclampsia: A Systematic Evidence Review for the U.S. Preventive Services Task Force. In www.ncbi.nlm.nih.gov. Agency for Healthcare Research and Quality (US). https://www.ncbi.nlm.nih.gov/books/NBK447464/
5 Townsend R, Khalil A, Premakumar Y, et al. Prediction of preeclampsia: review of reviews. Ultrasound Obstet Gynecol 2019;54:16-27.

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Can we use **arterial stiffness measurements** to better **predict the development of *preeclampsia*** – and furthermore, the ***type*** that will develop **(preterm, term, postpartum)** to create an opportunity for personalized prevention plans for each pregnancy?

Filling the knowledge gap...

REVEAL
n = 236
MUHC & JGH

→

PULSE
n = 2400
9+ Hospital Institutions incl. MUHC, JGH, CHU Ste-Justine

→

Ad hoc analysis
Using data from REVEAL and prospective data from PULSE
5 ML algorithms: *Support Vector Machine (SVM), Random Forest, Logistic Regression, Gradient Boosting, K-nearest Neighbours*

Pilot Study
Found that arterial stiffness had promising predictive ability of preeclampsia

Validation Study
Ongoing!

Filling the knowledge gap...

* Simplified overview of the study protocol

Recruitment of high-risk pregnancies
1 major risk factor OR
2 moderate risk factors

Follow-up Trimester 1
10-14 weeks gestation
Arterial stiffness measurement, questionnaires, blood draw, urine collection

Follow-up Trimester 2
18-22 weeks gestation
Arterial stiffness measurement, questionnaires, blood draw, urine collection

Follow-up Post-Partum
(Substudy, optional)
6-12 weeks post-partum
Arterial stiffness measurement, questionnaires, blood draw, urine collection

Monitoring for the development of PrE...

High Risk Factors	Moderate Risk Factors
• Autoimmune disease • Diabetes Mellitus type 1 or 2 • Chronic hypertension • Hypertensive disorder in a previous pregnancy • Chronic kidney disease • Placental-mediated complications of pregnancy in a previous pregnancy	• Nulliparous • Assisted reproduction (including IVF) • Family history of preeclampsia • African-American race • Sleep apnea • Connective tissue diseases • BMI >30 kg/m2 • Age ≥35 y

Table 1. Screening eligibility factors

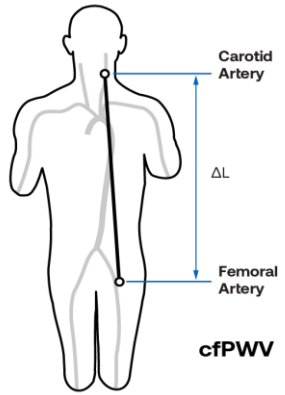

Fig 1. Illustration of the calculation of Pulse Wave Velocity from Sphygmocor Technology

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Background
- What is PrE?
- Types of PrE
- Knowledge gap

Methods
- REVEAL & PULSE
- Machine learning design

Results

Conclusions
- Future research

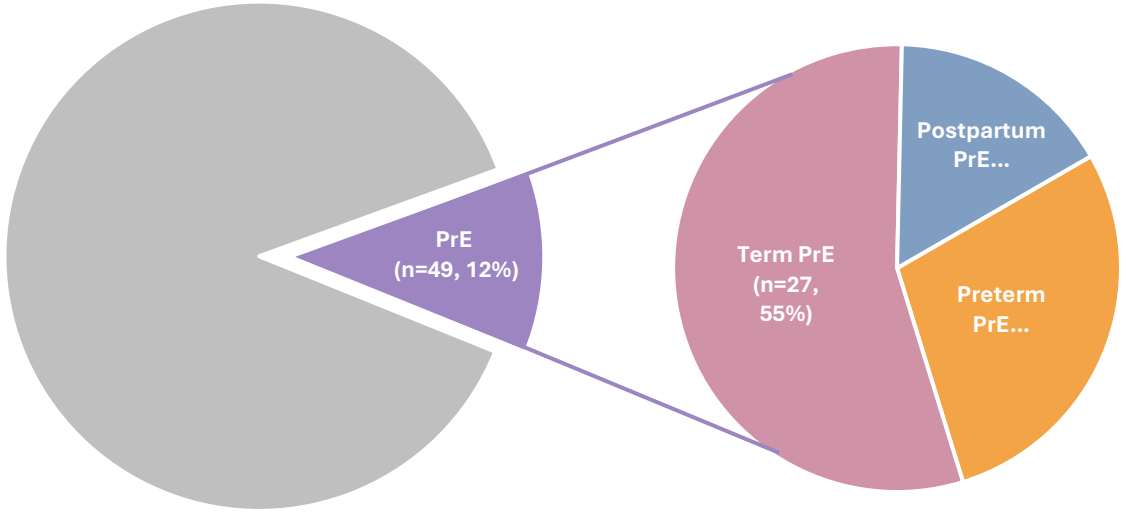


Figure 2. Cohort Statistics

	Best Performing Model (AUC)	
	Trimester 1	**Trimester 2**
PrE	0.75	0.74
Preterm PrE	0.74	0.63
Term PrE	0.79	0.71
Postpartum PrE	0.82	0.69

Table 2. Summary of Best Performing Models' AUC

Analysis of 14 Vascular Health Variables: cfPWV, T1R, AP, Aix, pSBP, pDBP, pPP, MAP, cSBP, cDBP, cPP, SEVR, HR, PPA

Figure 3a. ROC Curves for **PrE**

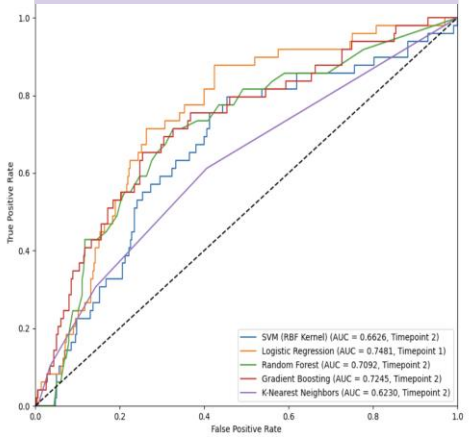


Figure 3b. ROC Curves for **Preterm PrE**

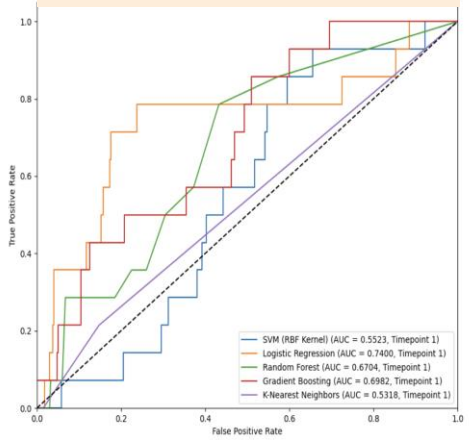


Figure 3c. ROC Curves for **Term PrE**

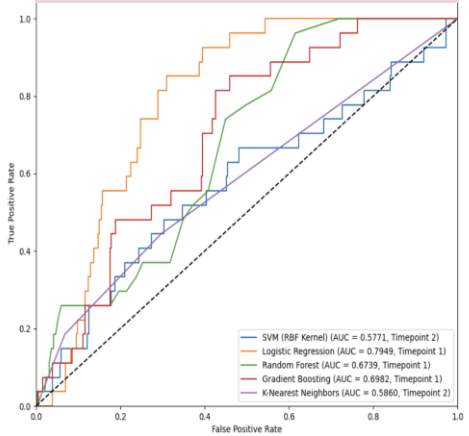
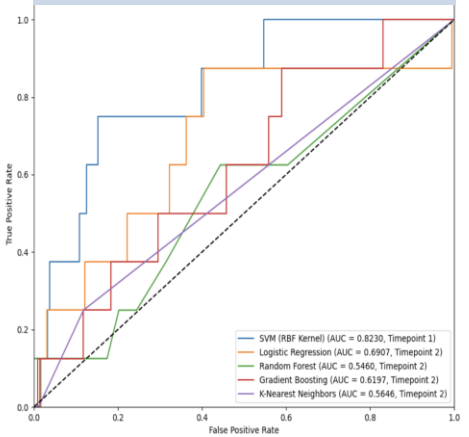


Figure 3d. ROC for **Postpartum PrE**



Conclusions

Arterial Stiffness was shown to have **high predictive ability for preeclampsia and its subtypes** as soon as the first trimester in pregnancy with highest values for term and postpartum preeclampsia.

Future Research

- Continue **expanding the cohort**
- Consider the *additive* predictive ability of AS measurements in **1st & 2nd trimester**
- Consider the *additive* predictive ability of AS with other **clinical, imaging and biological markers**

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