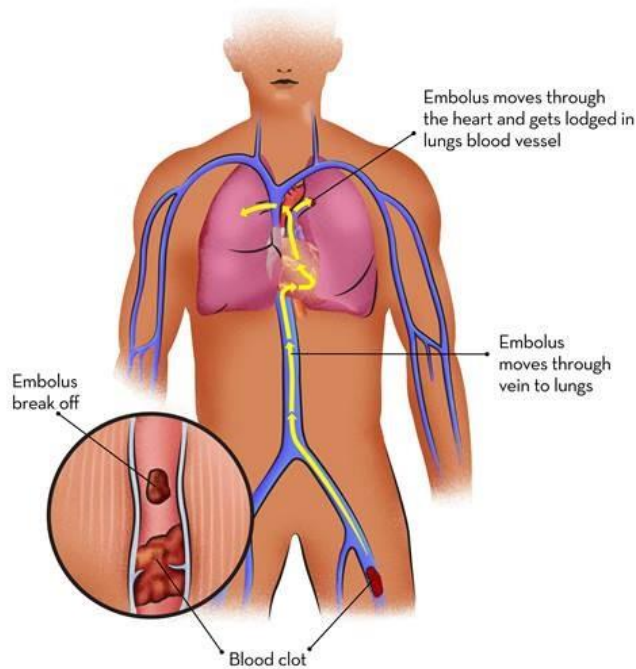


GLYCEMIC INDICES AND RELATED BIOMARKERS IN PULMONARY EMBOLISM

Roumika Patil



BACKGROUND ON PULMONARY EMBOLISM



- PE, also known as pulmonary embolism, is the blockage of pulmonary arteries in the lungs by a blood clot. This is often caused by an embolus that has traveled up to the lungs.
- Affects between 60-70 for every 100,000 in the US today
- Symptoms may include chest pain, fatigue, weakness, and shortness of breath

AIM/PURPOSE

- To analyze the correlation between inflammatory and glycemc biomarkers and thrombosis
- To assess the variance of D-Dimer, CRP, PAI-1, tPA, TAFI, vWF, and endogenous GAGs compared with a control population

MATERIALS/METHODS

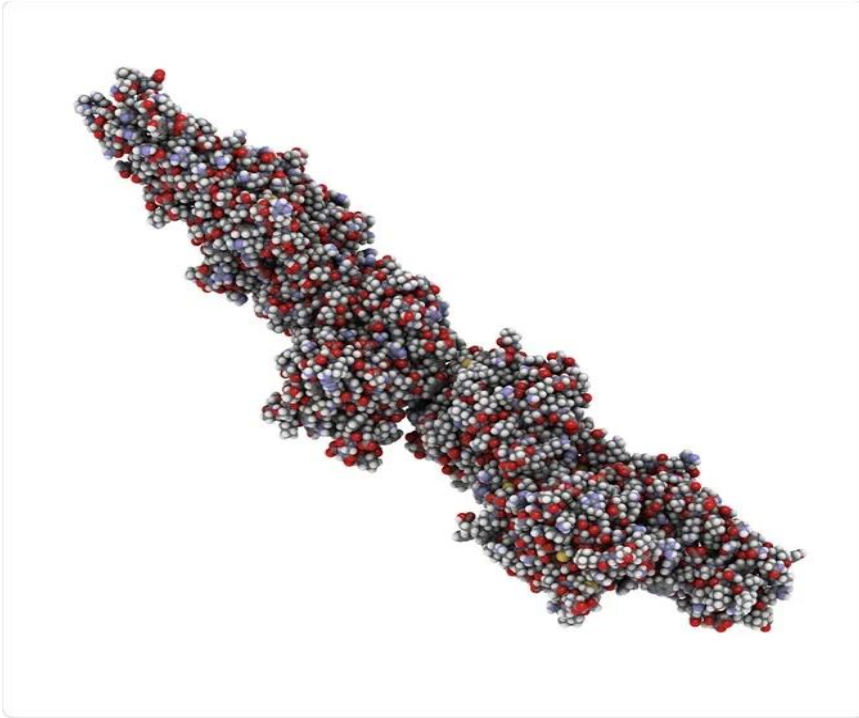
- Whole blood samples were collected from patients with confirmed diagnosis of PE
- Control Human Plasma (CHP) were obtained from commercially available source (George King Biomedical Center).
- Samples were processed through centrifuge to achieve platelet poor plasma and then stored at -70 degrees Celsius.
- Samples were analyzed using sandwich ELISA and Heparin Red methods
- Concentrations of biomarkers were statistically analyzed using Excel, GraphPad Prism, and IBM SPSS.

HYPOTHESIS

Pulmonary embolism patients will have significant associations with inflammatory and glycemic biomarkers when compared to a control population

D-DIMER ANALYSIS

BACKGROUND ON D-DIMER



Structure

- Small protein fragment consisting of α , β , and γ peptide chains

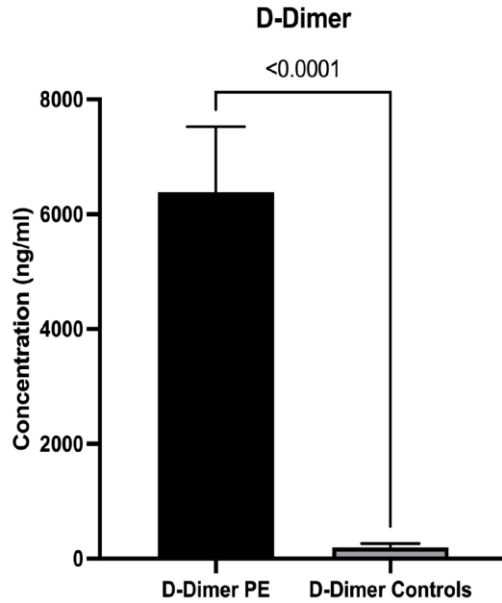
Production

- Made when blood clots dissolve

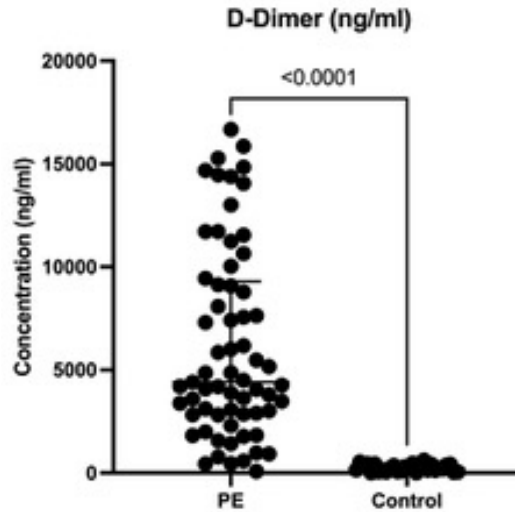
Correlation to PE

- High D-Dimer levels suggest some sort of blood clotting condition

D-DIMER RESULTS



N= 87

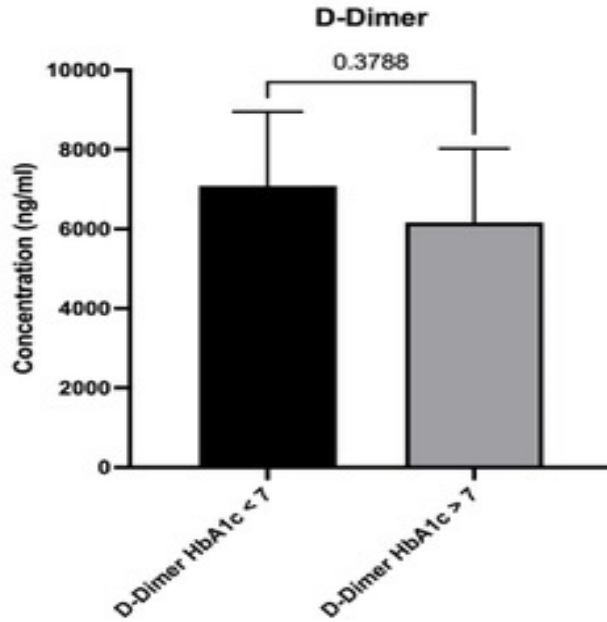


N= 115

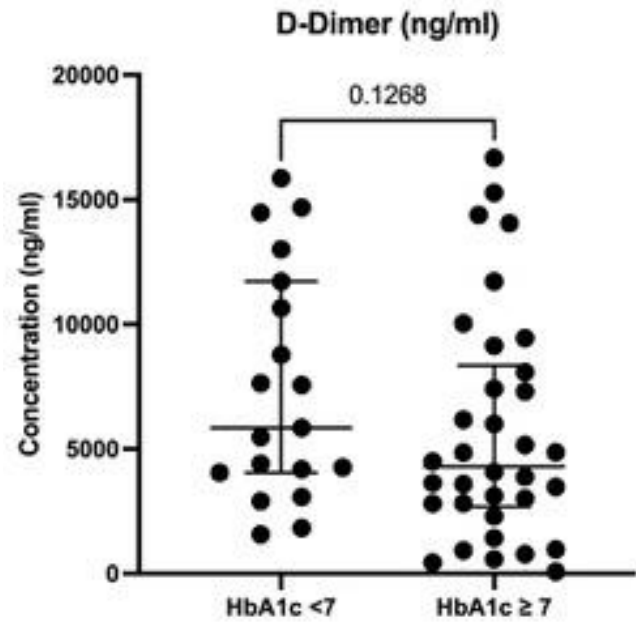
Percentiles (N = 87)	PE Patients	Control Plasma
25%	2814.66	4.65
50%	4855.61	126.17
75%	9543.49	368.41

Percentiles (N = 115)	PE Patients	Control Plasma
25%	2835.27	4.65
50%	4410.04	126.17
75%	9233.37	369.09

D-DIMER RESULTS



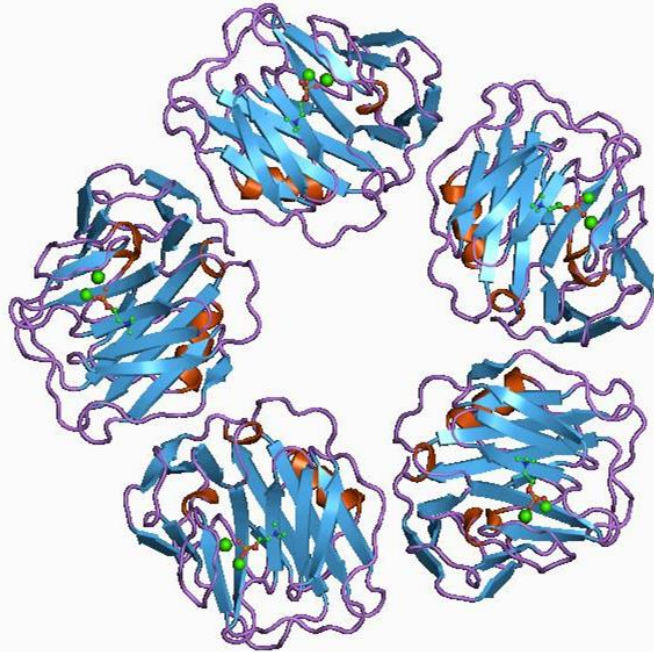
N= 87



N= 115

CRP ANALYSIS

BACKGROUND ON CRP



Structure

- cyclic pentameric protein comprised of five identical non-covalently attached subunits

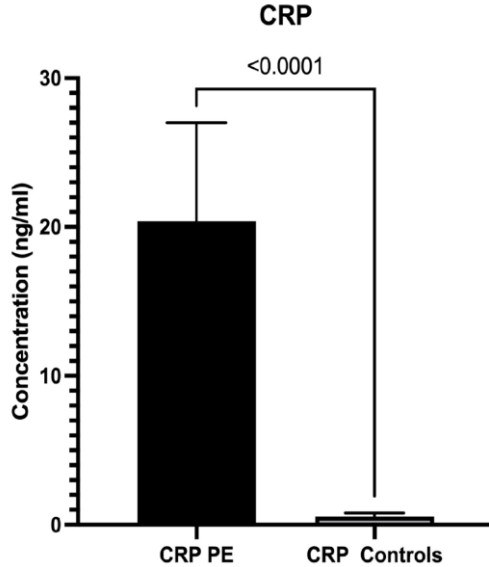
Function

- assist in complement binding to foreign and damaged cells

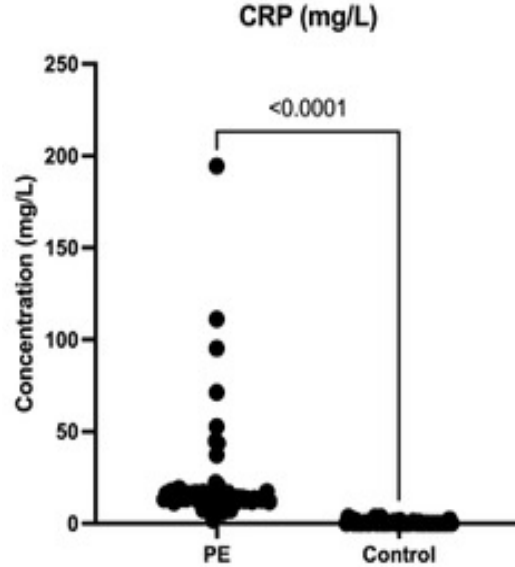
Correlation to PE

- High levels of CRP indicate acute inflammation

CRP RESULTS



N= 87

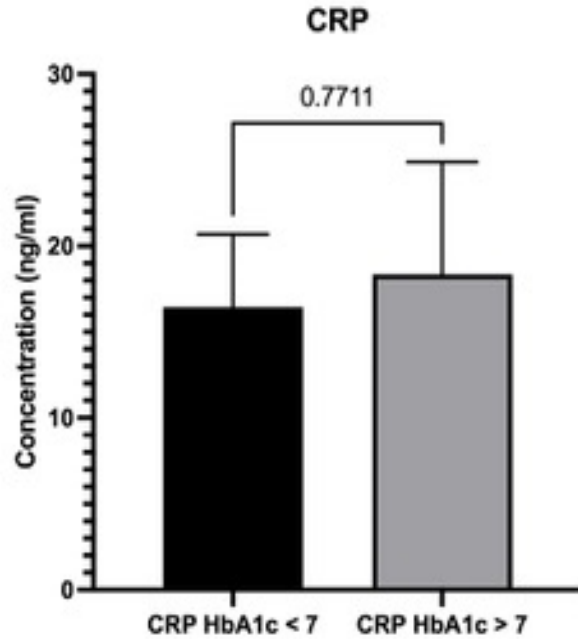


N= 115

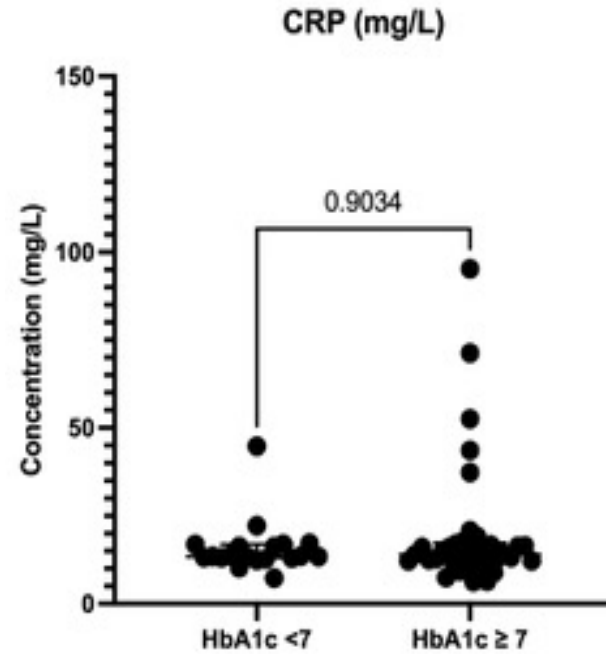
Percentiles (N = 87)	PE Patient	Control Plasma
25%	12.08	0.00
50%	13.26	0.11
75%	16.77	0.74

Percentiles (N = 115)	PE Patient	Control Plasma
25%	12.13	0.00
50%	13.42	0.07
75%	16.90	0.64

CRP RESULTS



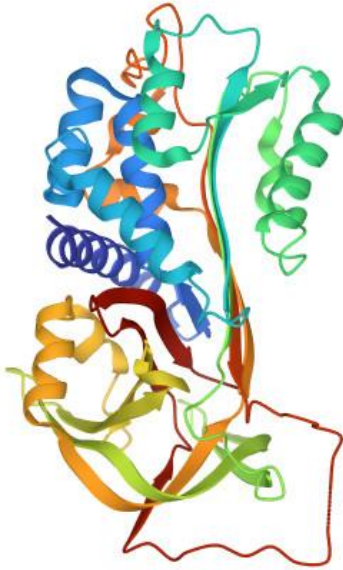
N= 87



N= 115

PAI-1 ANALYSIS

BACKGROUND ON PAI-1



Structure

- a single chain glycoprotein member of the superfamily of serine-protease inhibitors

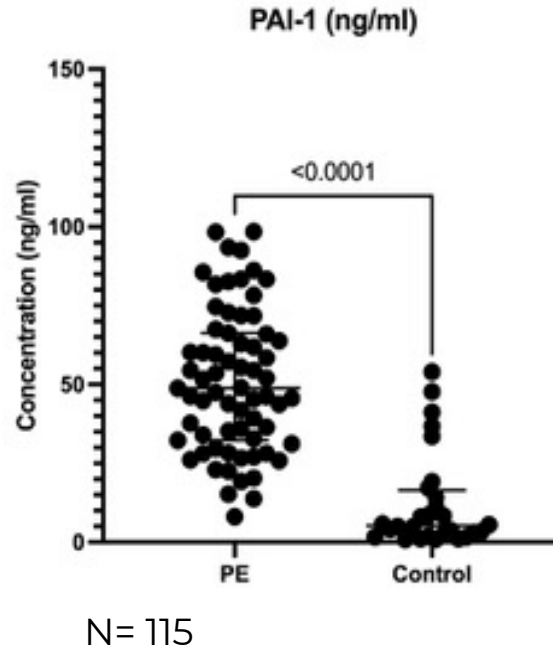
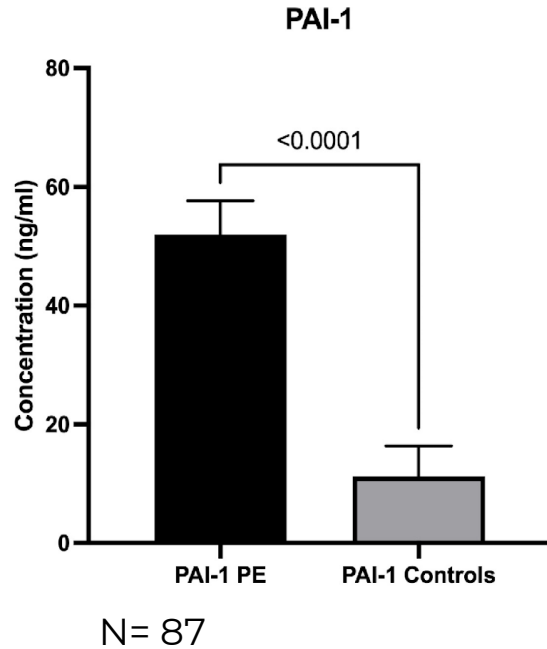
Function

- protein blocks (inhibits) the action of other proteins called plasminogen activators, which promote dissolution of clots

Correlation to PE

- High levels promote clotting

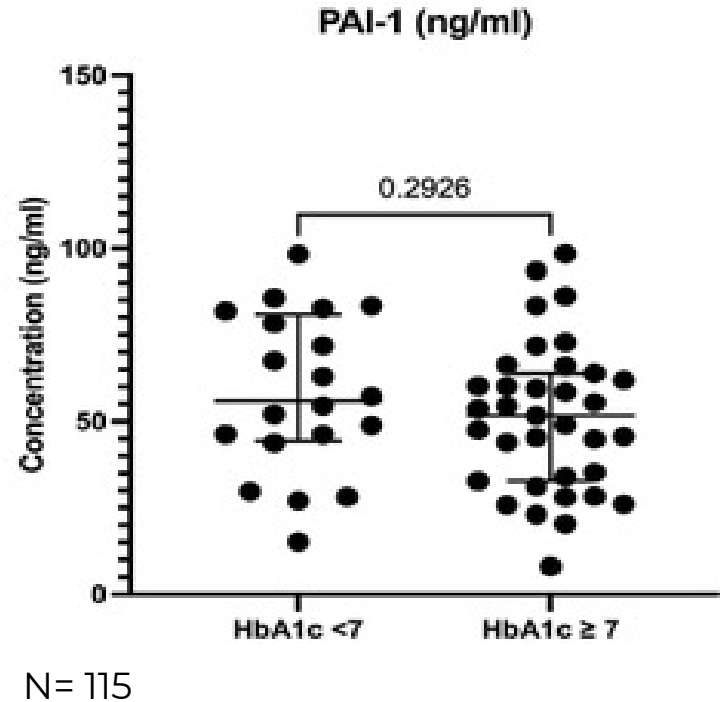
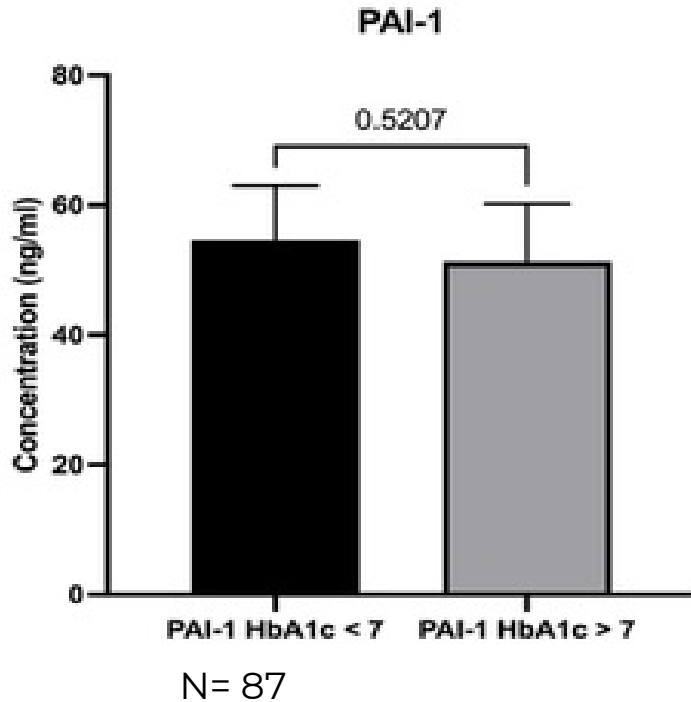
PAI-1 RESULTS



Percentiles (N = 87)	PE patient	Control plasma
25%	32.30	1.70
50%	49.01	4.96
75%	66.44	12.86

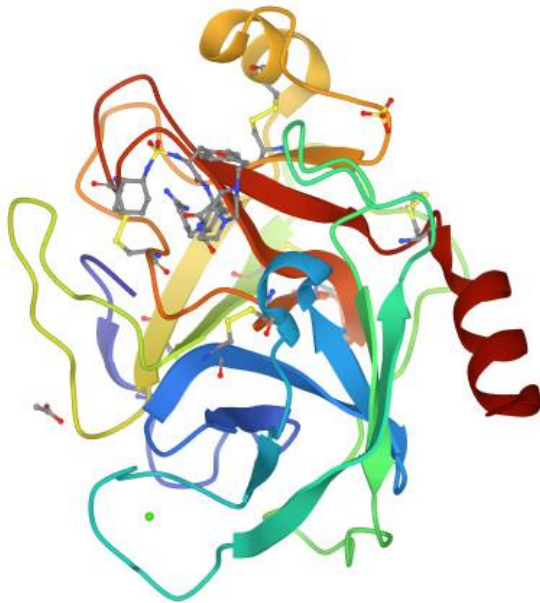
Percentiles (N = 115)	PE patient	Control plasma
25%	32.30	1.93
50%	48.82	5.23
75%	66.31	16.46

PAI-1 RESULTS



TPA ANALYSIS

BACKGROUND ON TPA



Structure

- Is composed of two chains; heavy A-chain and light B-chain

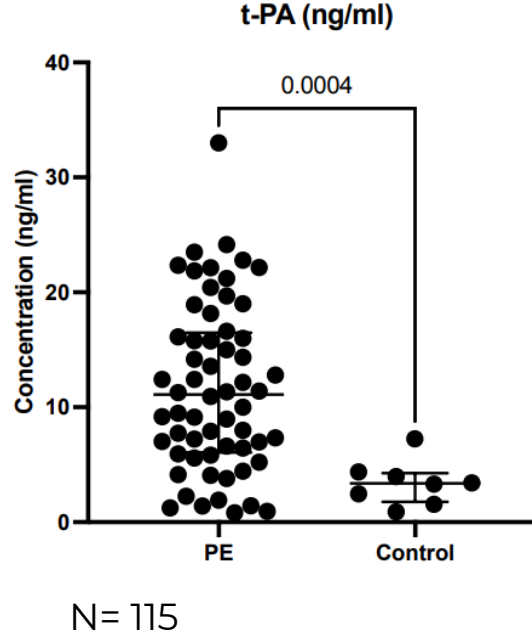
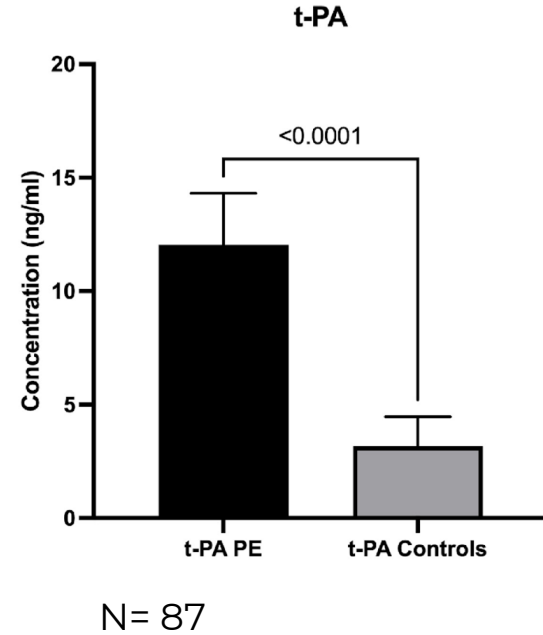
Function

- Catalyzes the conversion of plasminogen to plasmin

Correlation to PE

- Low tPA levels are associated with hypercoagulable states

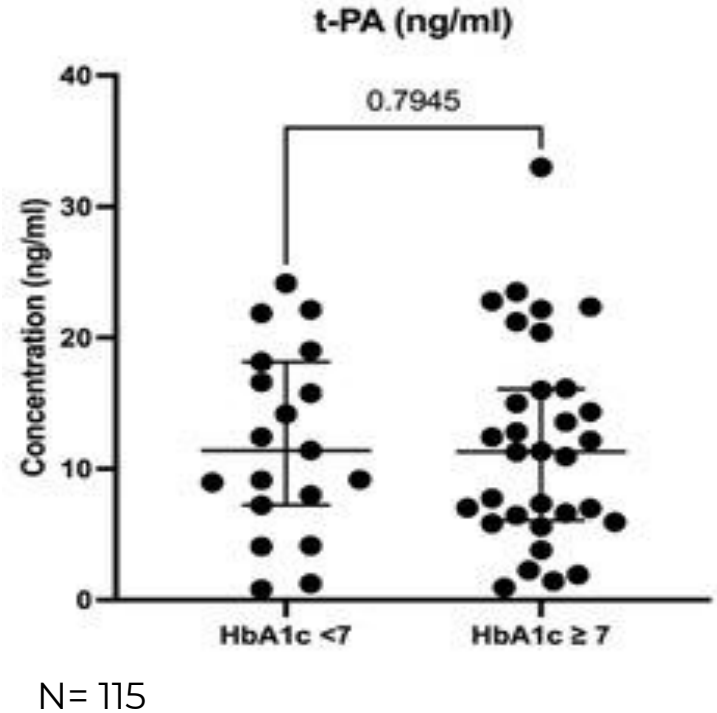
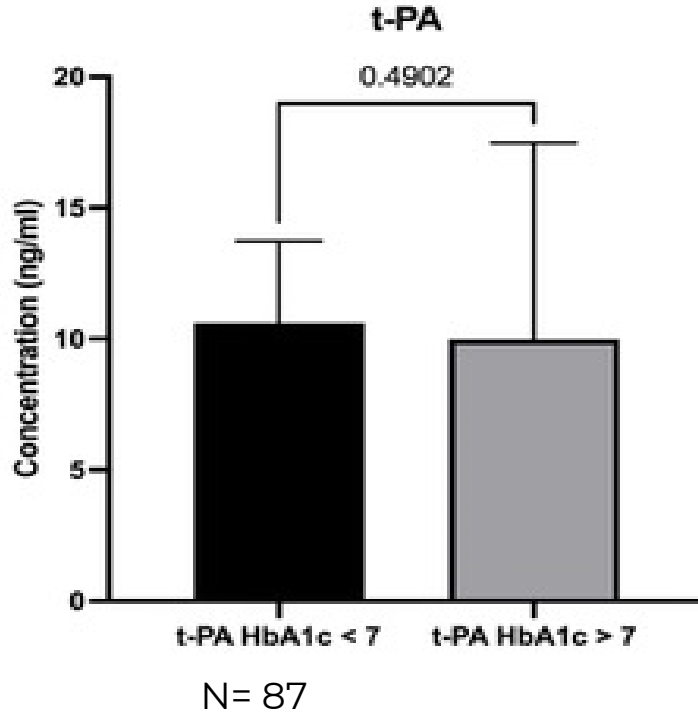
TPA RESULTS



Percentiles (N = 87)	PE Patient	Control Plasma
25%	6.10	1.64
50%	9.74	3.03
75%	16.58	4.07

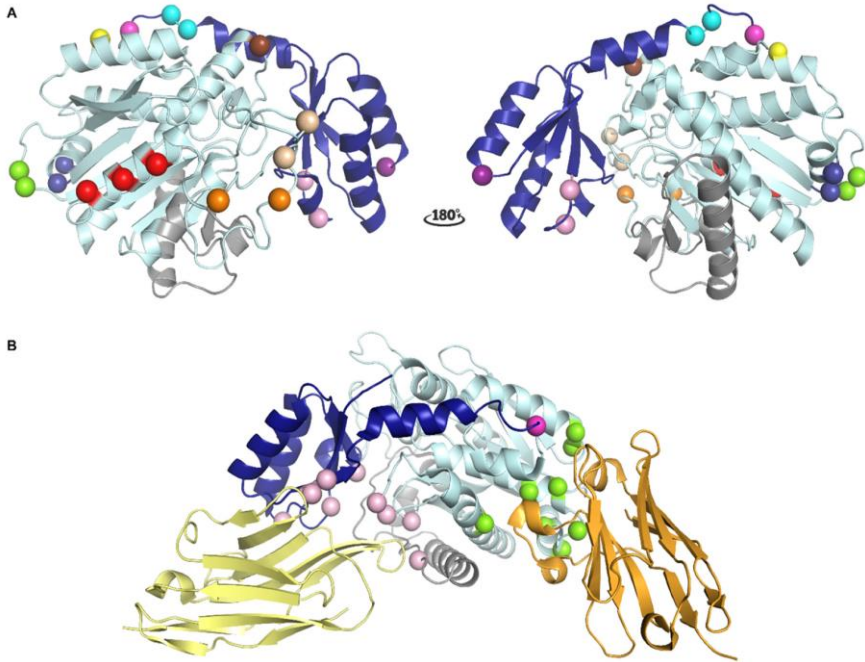
Percentiles (N = 115)	PE Patient	Control Plasma
25%	6.06	1.78
50%	11.11	3.37
75%	16.49	4.27

TPA RESULTS



TAFI ANALYSIS

BACKGROUND ON TAFI



Production

- Glycoprotein secreted by the liver

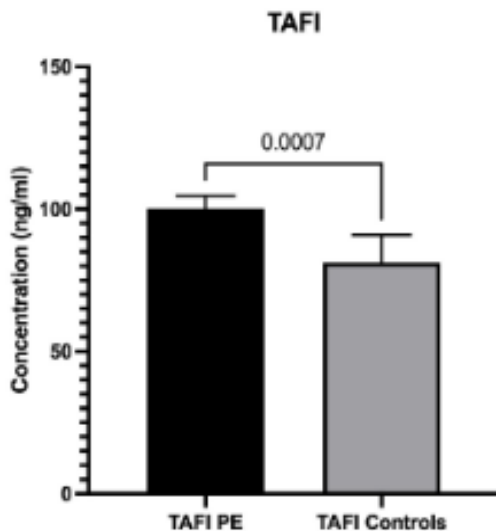
Function

- Suppresses fibrinolysis by removing certain residues from fibrin clots

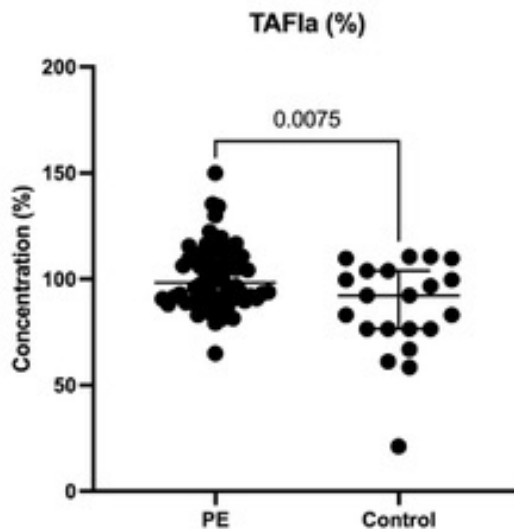
Correlation to PE

- High levels of TAFI are associated with high VTE incidence

TAFI RESULTS



N= 87

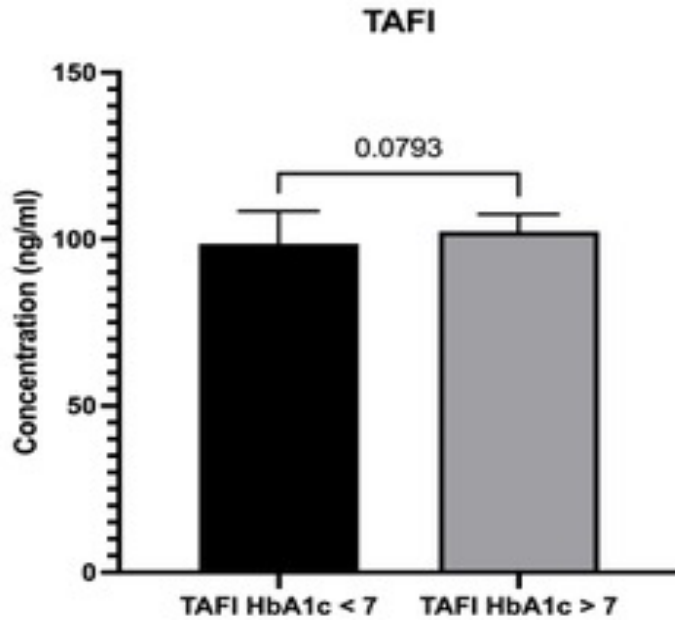


N= 115

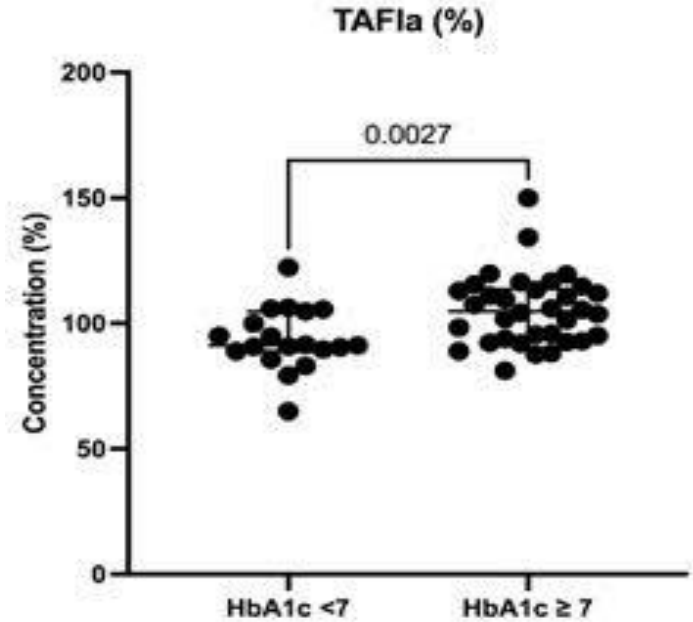
Percentiles (N = 87)	PE patient	Control plasma
25%	90.05	66.85
50%	97.85	83.11
75%	109.47	99.65

Percentiles (N = 115)	PE patient	Control plasma
25%	90.74	76.48
50%	98.30	92.31
75%	110.87	103.91

TAFI RESULTS



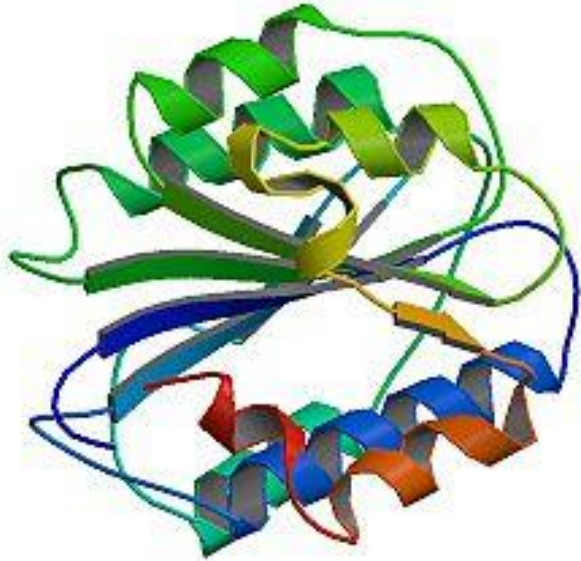
N= 87



N= 115

VWF ANALYSIS

BACKGROUND ON VWF



Structure

- Large multimeric glycoprotein present in plasma

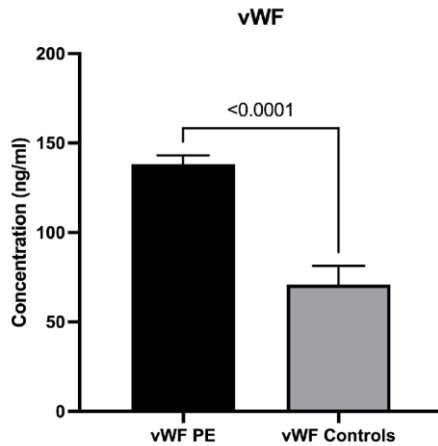
Function

- Helps platelets stick together and stick to the blood vessel walls when wound is present

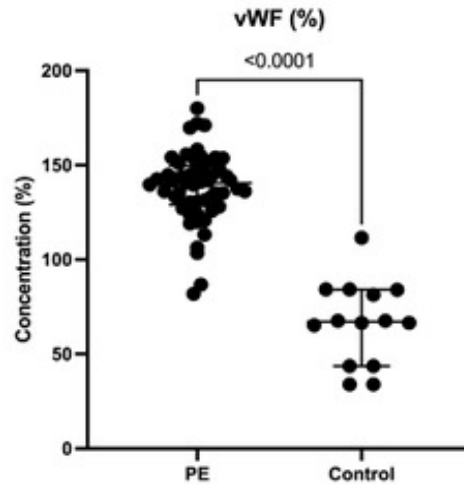
Correlation to PE

- High VWF plasma levels are associated with increased risk of VTE or other related events

VWF RESULTS



N= 87

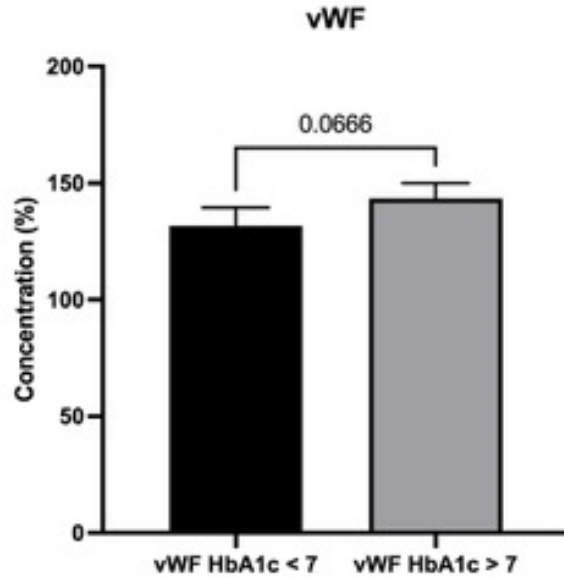


N= 115

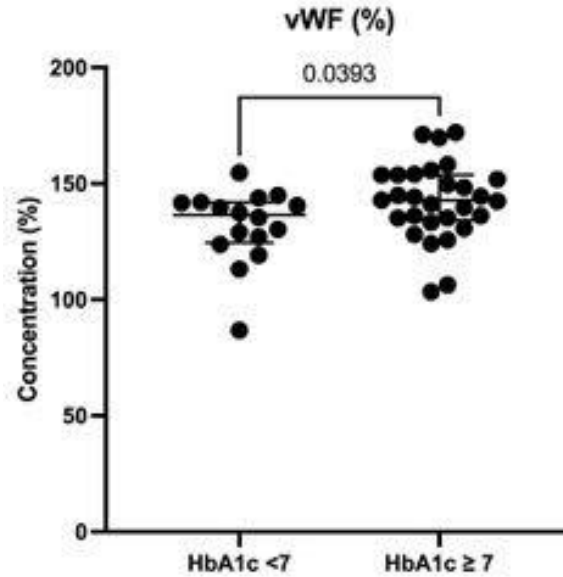
Percentiles (N = 87)	PE patients	Control plasma
25%	129.24	65.24
50%	139.73	57.64
75%	146.66	84.02

Percentiles (N = 115)	PE patients	Control plasma
25%	129.06	43.64
50%	140.56	67.10
75%	149.60	84.07

VWF RESULTS



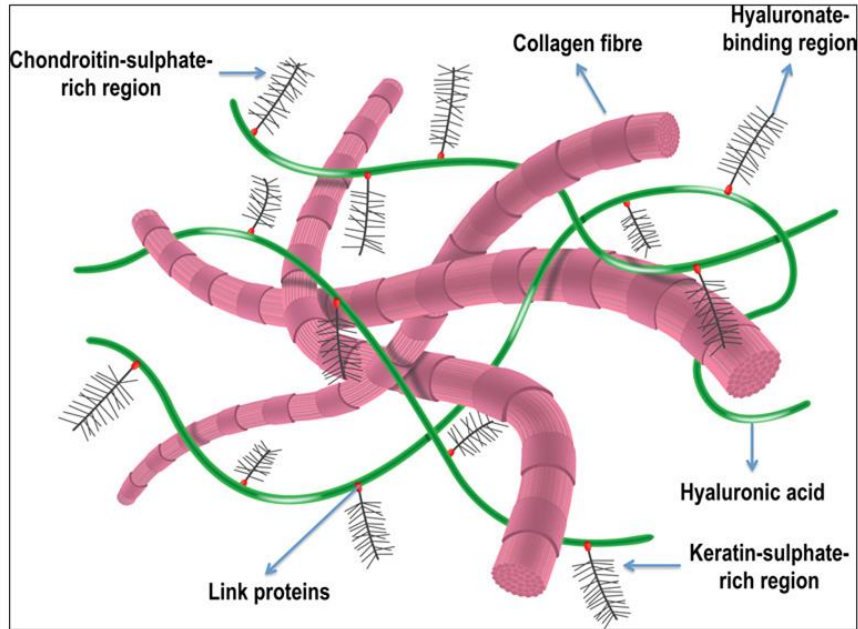
N= 87



N= 115

ENDOGENOUS GAGS ANALYSIS

BACKGROUND ON ENDOGENOUS GAGS



Structure

- Specific group of glycoprotein made in Golgi Apparatus

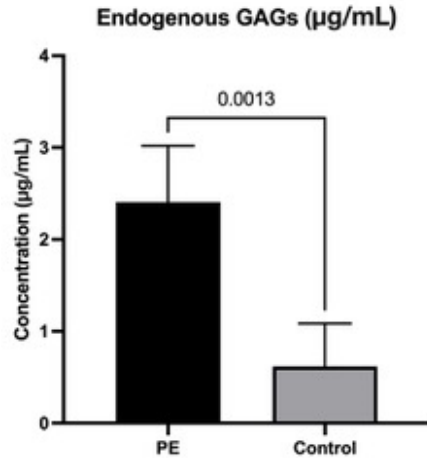
Function

- Widespread throughout body, including the cell signaling process

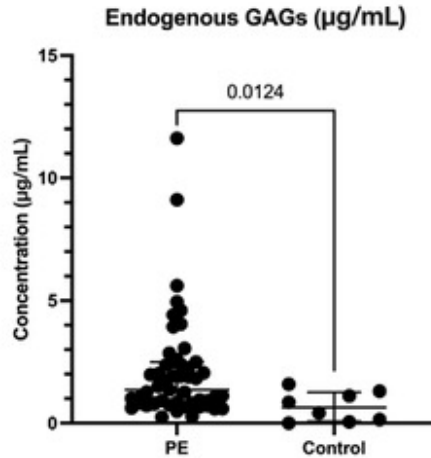
Correlation to PE

- Increased thrombo-inflammatory response associated with endogenous GAGS

ENDOGENOUS GAGS RESULTS



N = 87

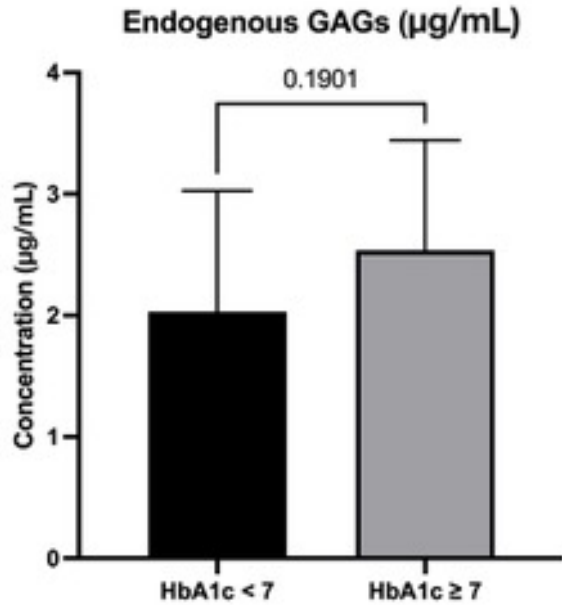


N = 115

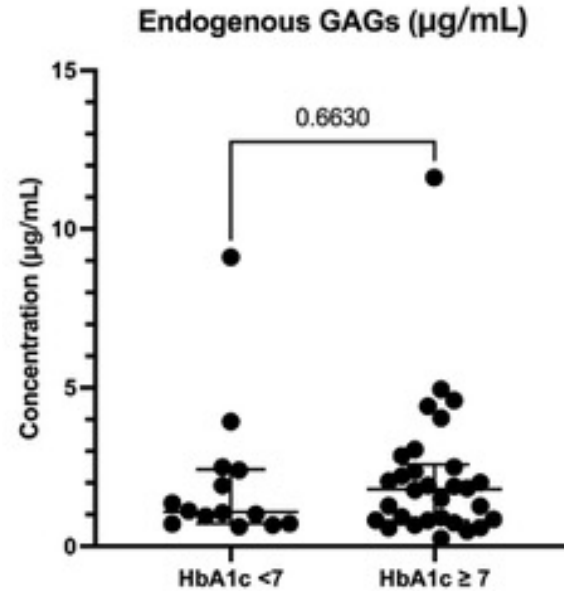
Percentiles (N = 87)	PE patients	Control plasma
25%	0.62	0.06
50%	1.83	0.42
75%	3.29	1.21

Percentiles (N = 115)	PE patients	Control plasma
25%	0.81	0.08
50%	1.36	0.64
75%	2.50	1.26

ENDOGENOUS GAGS RESULTS



N = 87



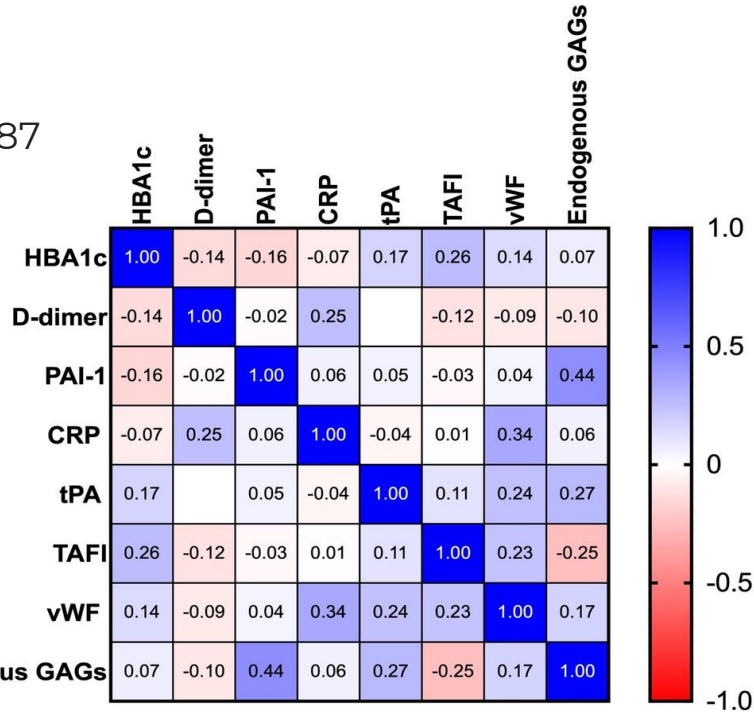
N = 115



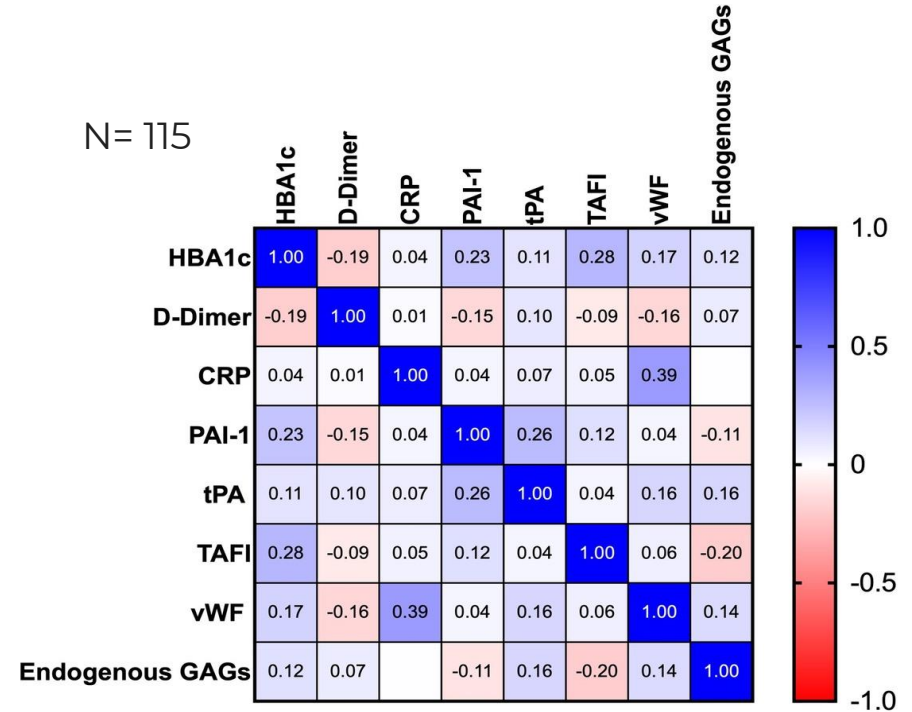
CROSS ANALYSIS

HEAT MAP RESULTS

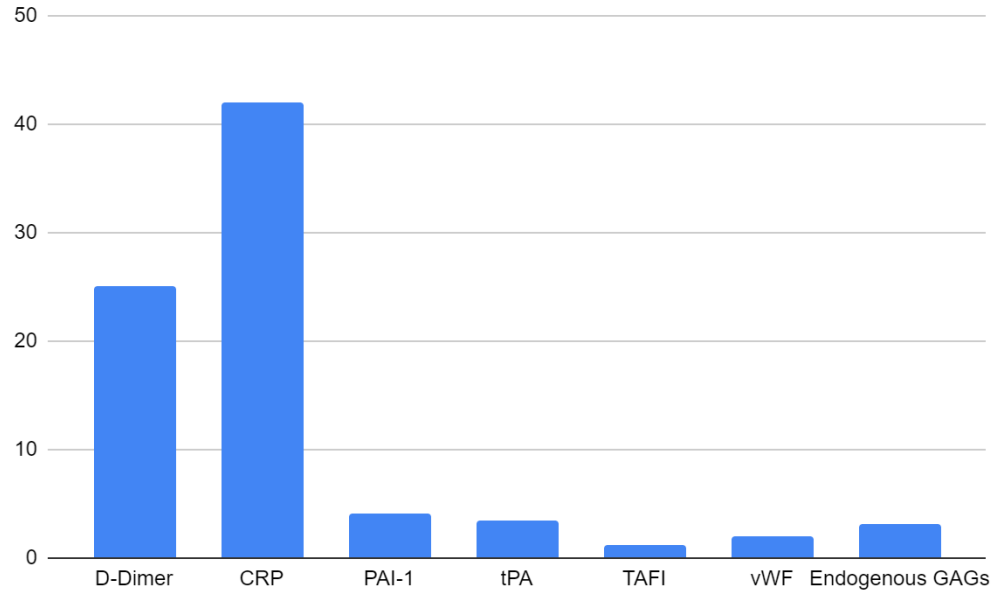
N= 87



N= 115



FOLD INCREASE COMPARISON



LIMITATIONS

In order to understand the complexity of glycemic control and other factors, we would have needed to do subgroup analyses and also needed a higher patient group population

CONCLUSION

- Our hypothesis was proven correct since there was a difference between the control and diabetic PE patient biomarker levels and some biomarkers had positive correlations between the two
- Further investigation is needed for a larger data set and understanding the role of glycemic control

NEXT STEPS

- submit abstract to ASH meeting
- submit abstract to FASEB
- possibly visit Loyola in October

ACKNOWLEDGEMENT

- I would like to thank Dr. Laddu, Dr. BK, Dr. Fareed, the Loyola staff, and GTF team for helping aid me during this project.

THANK YOU!

DO YOU HAVE ANY QUESTIONS?