Diagnostic and Prognostic Evaluation of Blood-Based Biomarkers in Chagas Disease

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Introduction

- Chagas Disease, caused by the Trypanosoma cruzi parasite effects 8-10 million people in Latin America. Most infected individuals remain asymptomatic while 30% develop Chagas Cardiomyopathy.
- Four proteins: Vimentin, 8-OHdG, Copeptin, and Endostatin showed excellent prognostic value for predicting disease severity in a 2021 study. [1]
- Mitochondrial dysfunction in cardiac tissue suggests that mitochondrial DNA could serve as a predictor of Chagas Disease presence and symptom status.[2]
- Our study evaluates both proteomic biomarkers and mtDNA copy number to assess their individual diagnostic and prognostic value in identifying Chagas Disease infection and stratifying disease progression.

Methods

- 42 randomly selected human participants enrolled and classified into three groups; 12 without Chagas disease (NHS: Normal Healthy Subjects), 15 with Chagas disease but asymptomatic (ASYM), 15 with Chagas disease and symptomatic (SYM).
- Blood samples were collected from each participant and levels of six protein biomarkers were measured in both serum and plasma and five mitochondrial biomarkers measured in serum.
- Performed two rounds of binary logistic regression with symptomatic status as one outcome and presence of Chagas disease as the other. Each protein biomarker was tested individually in serum and plasma and used as continuous predictors; mitochondrial DNA biomarkers were tested only in serum.
- Predicted probabilities from logistic models were used to generate Receiver Operating Characteristic (ROC) curves. Area Under the Curve (AUC) was computed to evaluate diagnostic accuracy for each biomarker. [Figures 1, 2]
- Ridge logistic regression was performed with 10-fold cross-validation to reduce overfitting and a dummy variable with near-zero variance was added to prevent dimensionality issues with single predictors.

Results

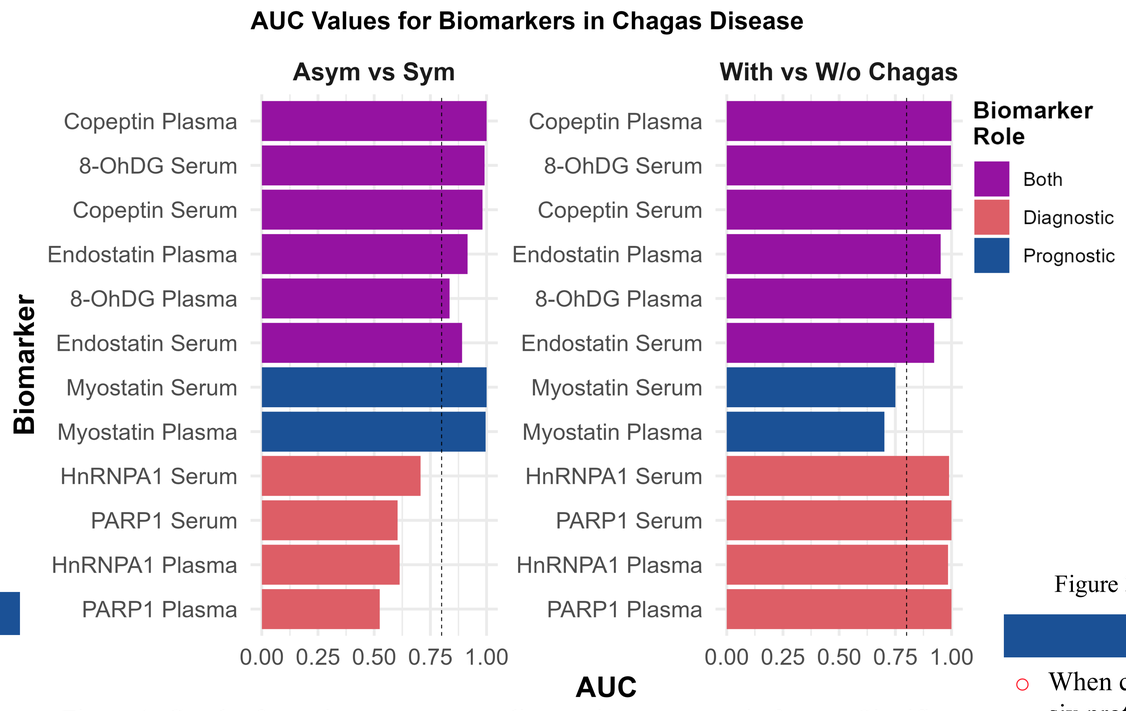

Figure 1: Graph of protein parameters as diagnostic or prognostic factors. Significant (AUC > 0.8)

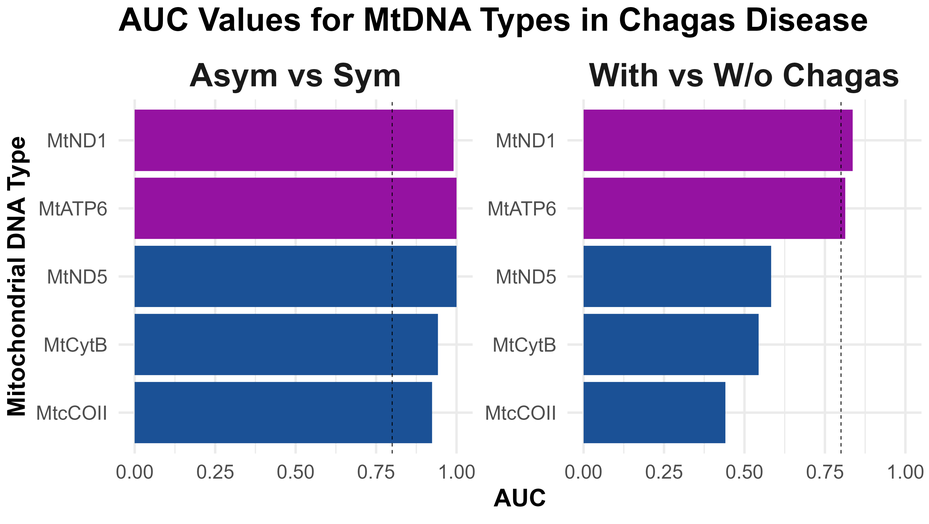

Figure 2. Graph of mtDNA types area under the curves. Significant (AUC > 0.8)

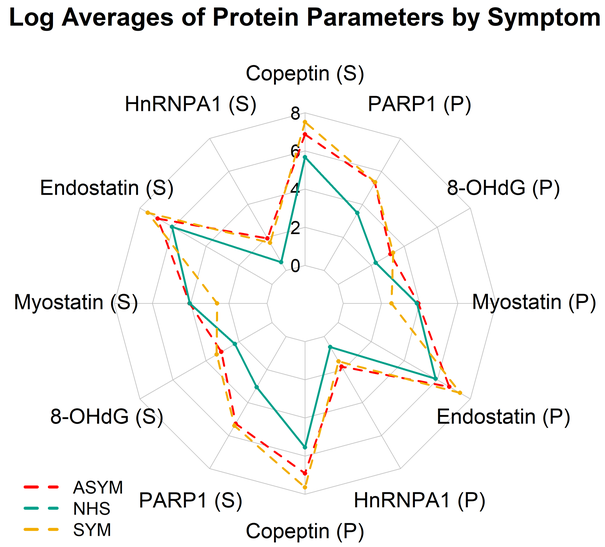

Figure 3: Radar plot of log averages of each protein parameter by symptom level

Discussion

- When comparing between individuals with or without Chagas disease, all six protein parameters measured in both serum and plasma showed significant positive predictive power, except for Myostatin, MTCytB and MtcCOII which demonstrated low AUC. [Figure 1, 2]
- When comparing asymptomatic vs symptomatic individuals with Chagas disease, all protein and MtDNA parameters were significant predictors except for HnRNPA1 and PARP1 in both serum and plasma, failing to significantly distinguish between the two clinical subgroups. [Figure 1, 2]

Conclusion

- HnRNPA1 and PARP1 levels in both serum and plasma were found to be diagnostic biomarkers for the presence of Chagas disease. [Figure 1] Myostatin levels in both serum and plasma were associated with disease progression, serving as a prognostic marker. [Figure 1] Copeptin, Endostatin, and 9-OHdG levels provide both diagnostic and prognostic information. [Figure 1]
- All 5 Mitochondrial DNA Types are strong prognostic biomarkers for Chagas Disease with AUC values >0.9. [Figure 2]. MtND1 and MtATP6 are moderate diagnostic biomarkers for Chagas Disease with AUC values > 0.8.[Figure 2]

References

1. **Choudhuri, S., Miller, L., Medvedovic, M., Rahhal, R., & Jones, D. P. (2021).** Prognostic performance of peripheral blood biomarkers in identifying seropositive individuals at risk of developing rheumatoid arthritis. Arthritis Research & Therapy, 23, Article 183.
2. **Bray, A. W., & Ballinger, S. W. (2017).** Mitochondrial DNA mutations and cardiovascular disease. *Current Opinion in Cardiology, 32*(3), 267–274.

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