

# ACC.26

## A Validation Study of Predictive Biomarkers for Diagnosis and Risk Stratification of Cardiogenic Shock among Patients Admitted to the Cardiac Intensive Care Unit

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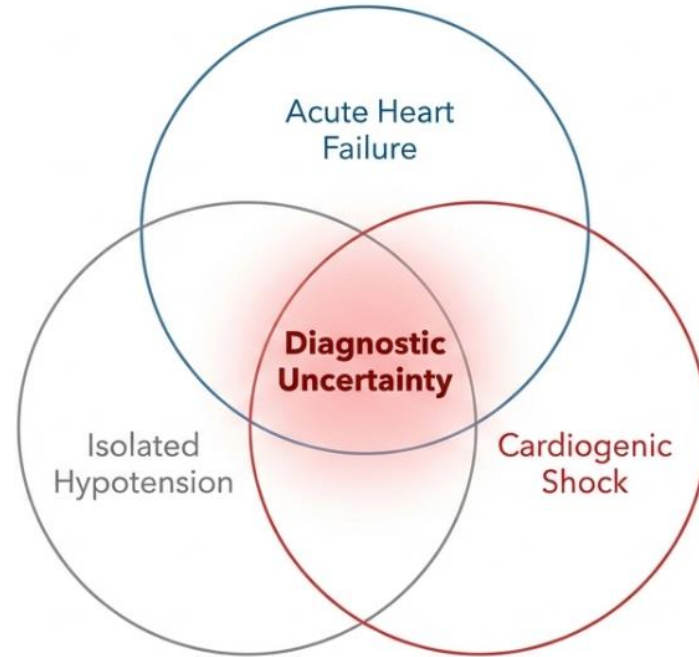
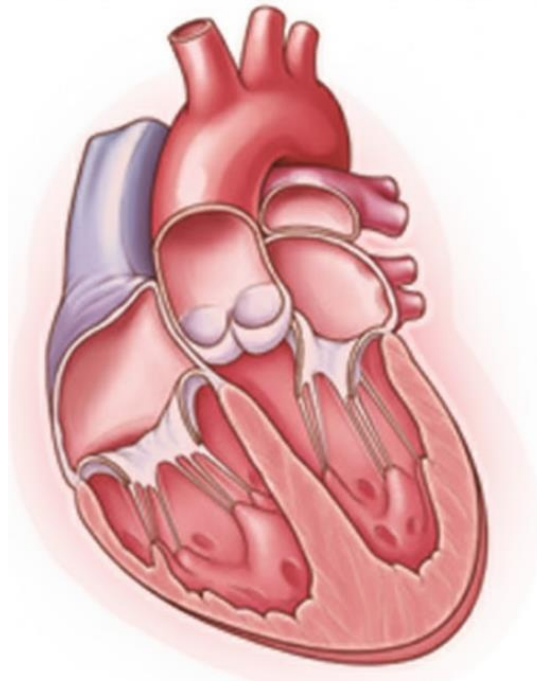
# Conflict of Interest Disclosure

Nicholas Chiu

*I have no financial relationships with a commercial entity producing healthcare-related products and/or services.*

# Background

## CARDIOGENIC SHOCK



**Mortality ranges from  
30-50%**

**Cardiogenic shock is  
heterogenous**

**Phenotyping may improve  
diagnosis, risk stratification,  
and personalize therapies**



# Initial Pilot Study (2024)



**ESC**

European Society  
of Cardiology




European Heart Journal: Acute Cardiovascular Care (2024) **13**, 624–628

<https://doi.org/10.1093/ehjacc/zuae068>

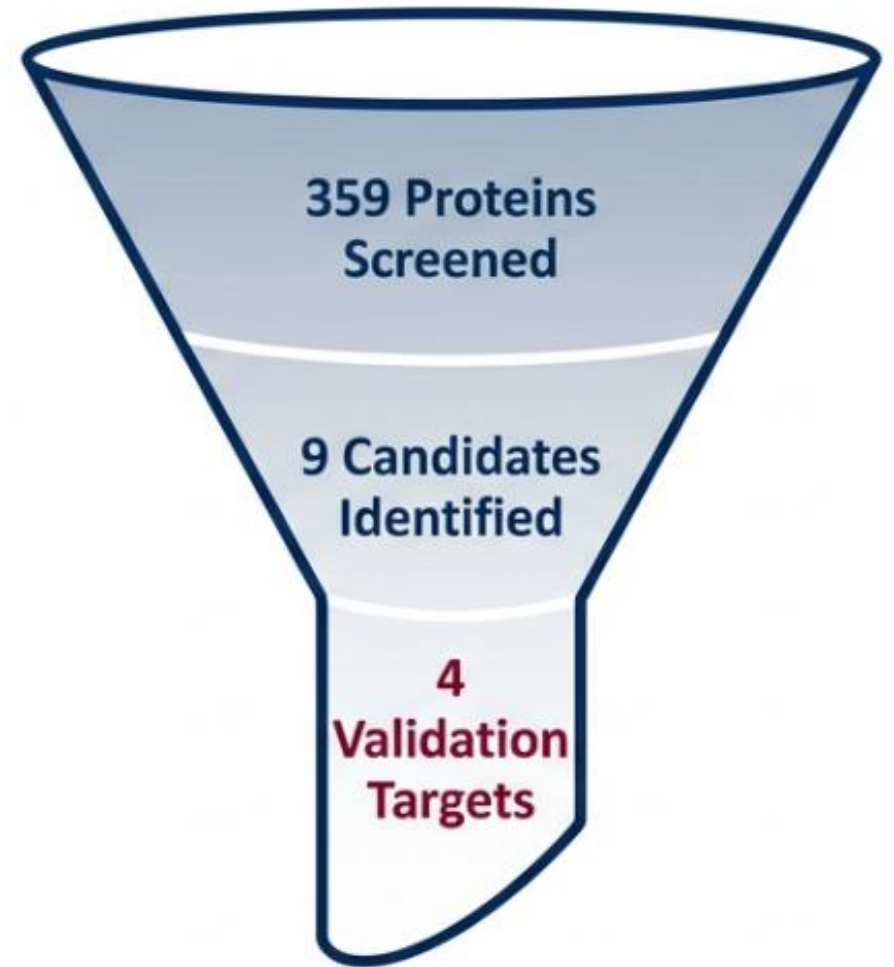
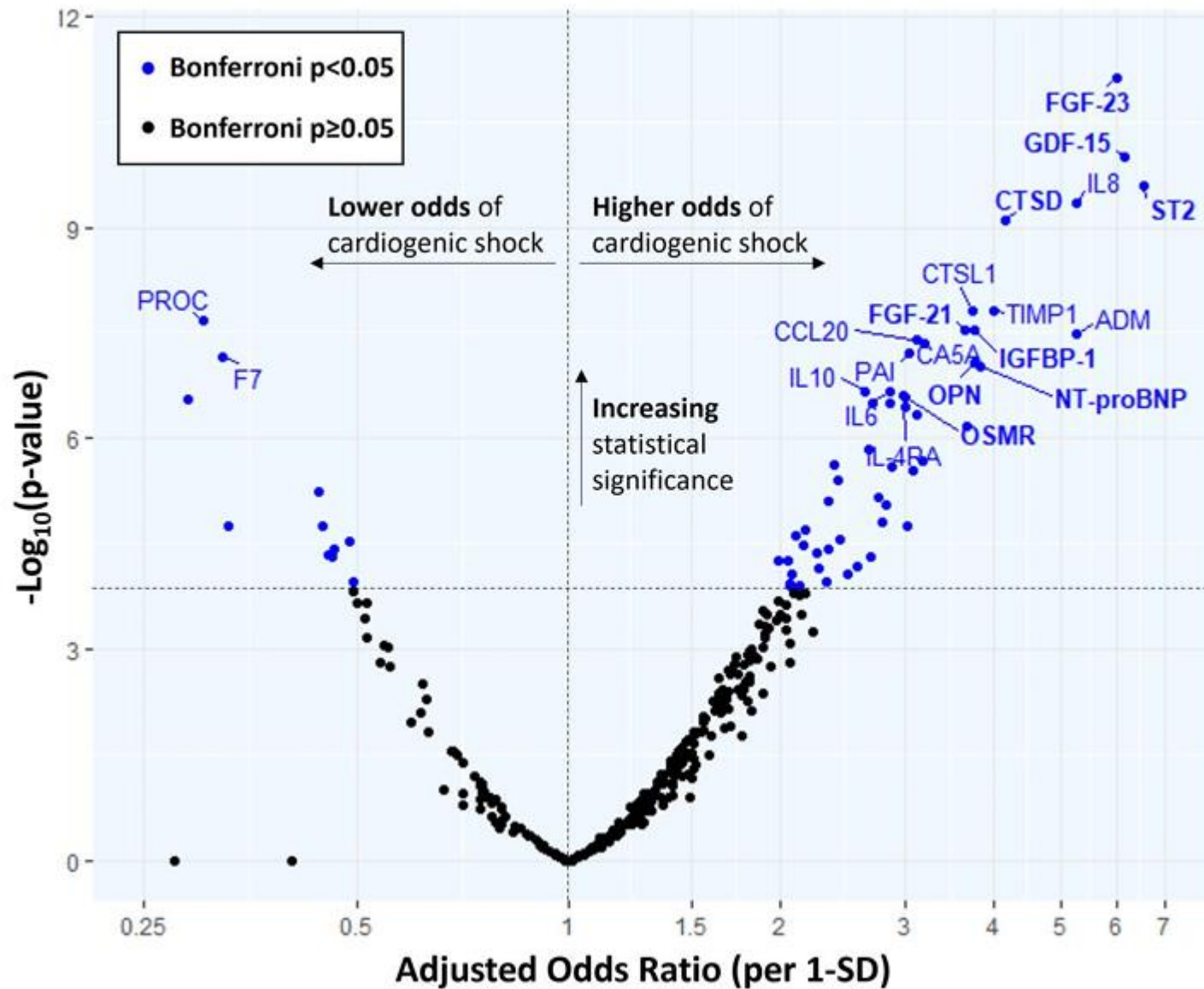
**BRIEF REPORT**

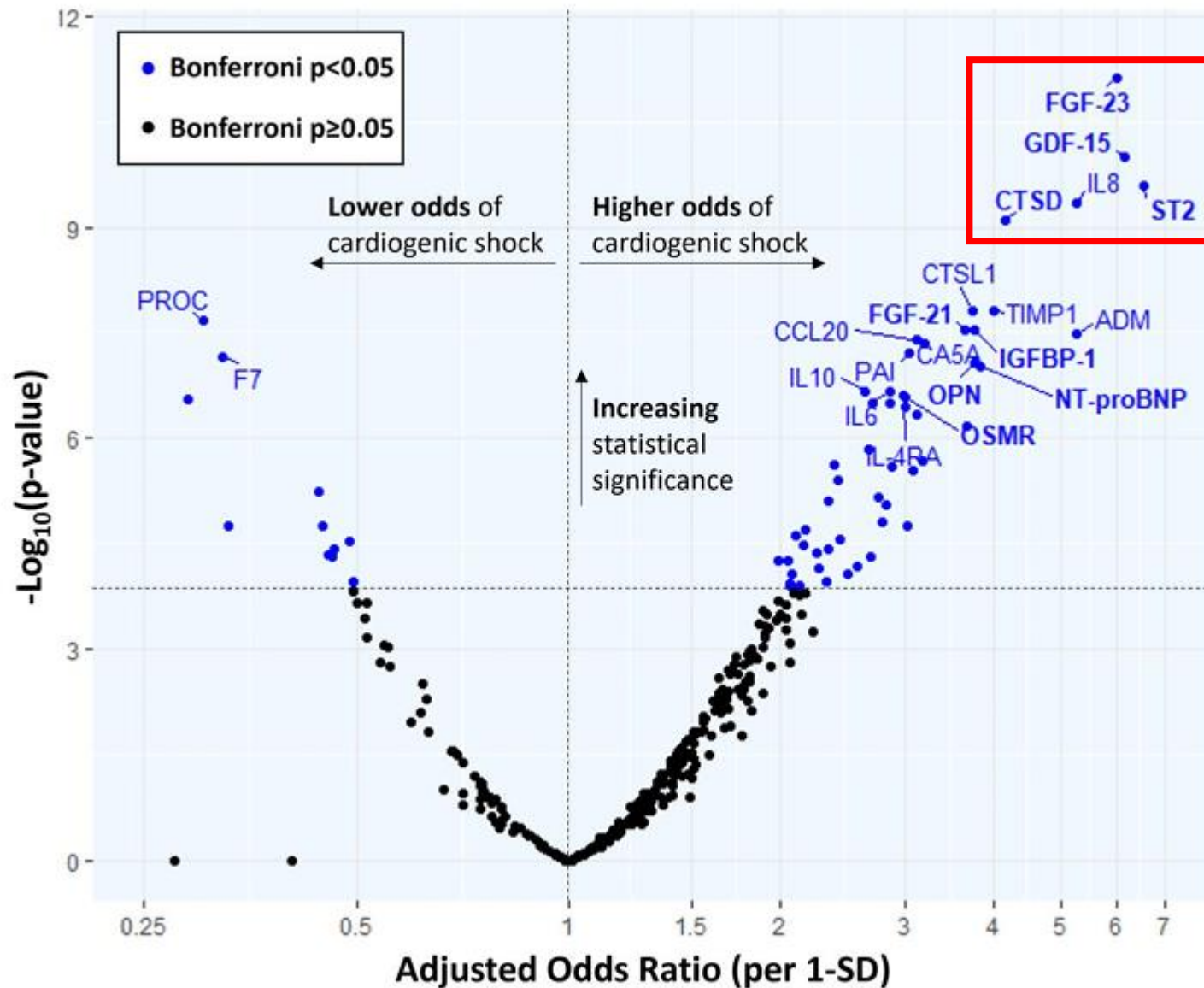
*Heart Failure and Cardiomyopathies*

## Targeted proteomic profiling of cardiogenic shock in the cardiac intensive care unit

Siddharth M. Patel <sup>1†</sup>, Mathew S. Lopes<sup>1†</sup>, David A. Morrow<sup>1</sup>, Andrea Bellavia<sup>1</sup>, Ankeet S. Bhatt<sup>2</sup>, Kayleigh K. Butler<sup>1</sup>, Jessica D'Antonio<sup>3</sup>, Michael Dunn<sup>3</sup>, Antonio A. Fagundes Jr<sup>4</sup>, Petr Jarolim <sup>5</sup>, Ethan P. Marin<sup>3</sup>, Lori Morton<sup>3</sup>, Benjamin A. Olenchock<sup>3</sup>, Balimkiz Senman<sup>6</sup>, Danuzia S. da Silva<sup>7</sup>, Anubodh S. Varshney<sup>8</sup>, Erin A. Bohula<sup>1‡</sup>, and David D. Berg <sup>1\*‡</sup>

**ACC.26**





**4 predictive biomarkers** were significant in an **adjusted multi-marker model** and further selected for **validation**:

- FGF-23**
- GDF-15**
- sST2**
- CTSD**

\*IL-8 was not independently associated with cardiogenic shock when compared with hypotension controls

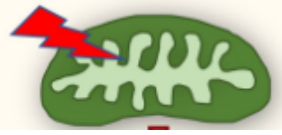
**FGF-23**

*Fibroblast Growth Factor-23*



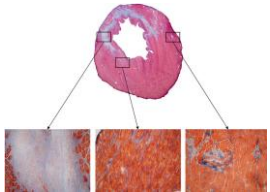
**GDF-15**

*Growth Differentiation Factor-15*



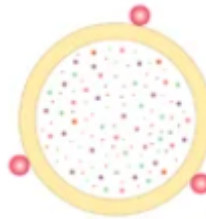
**Our present study:**

**Validation of our 4-biomarker panel in a larger  
CICU cohort...**



**sST2**

*soluble Suppression of Tumorigenicity-2*



**CTSD**

*Cathepsin D*

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# Study Aims



## 1. Discriminate

Can these markers accurately diagnose CS vs. non-shock controls?



## 2. Differentiate

Can they distinguish CS from other shock phenotypes (e.g., Distributive)?



## 3. Prognosticate

Do they predict mortality independent of other clinical characteristics?

FGF-23

## Population

GDF-15



**254**

**Cardiogenic Shock  
Cases**

**170** *Persistent CS*

**84** *Supported CS*

sST2

CTSD

**ACC.26**

FGF-23

GDF-15

# Population

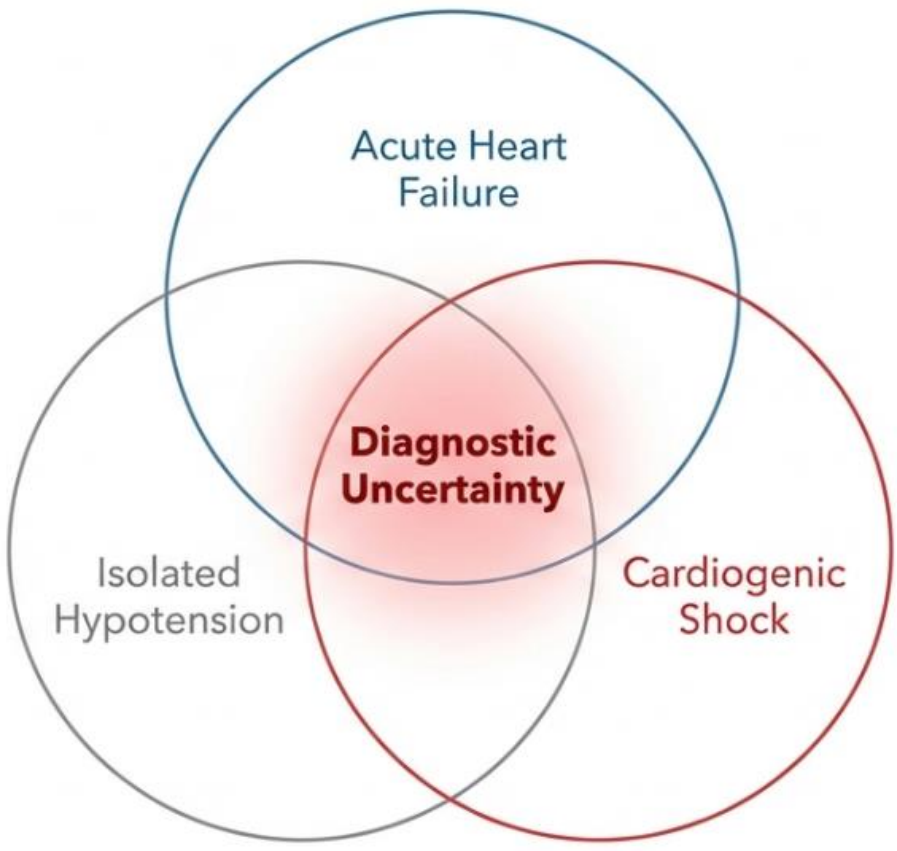


**254**

**Cardiogenic Shock Cases**

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sST2

CTSD

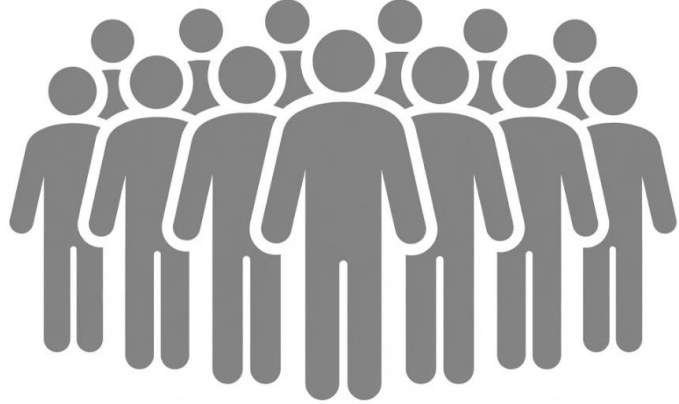
# Population



**254**

**Cardiogenic Shock Cases**

*170 Persistent CS*  
*84 Supported CS*



**619**

**Controls**



**Heart Failure Controls**



**Hypotension Controls**



**Other Non-Shock Controls**

FGF-23



254

Cardiogenic Shock Cases

170 Persistent CS  
84 Supported CS

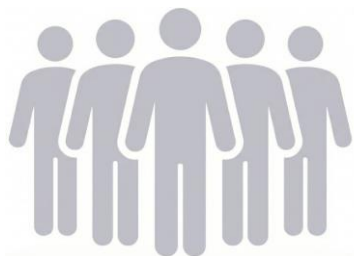
sST2

# Population



619

Controls



Heart Failure Controls



Hypotension Controls



Other Non-Shock Controls

GDF-15



70

Distributive Shock Cases

\*Mixed shock was excluded to allow comparisons between hemodynamically distinct shock subtypes

CTSD

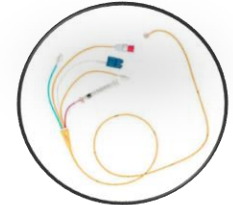
# Biomarker Draw and Adjudication



**Biomarker samples drawn on  
CICU admission**



**Shock classification by physician  
adjudication within 6 hours of draw**



# Statistical Methods

## Diagnostic Analysis

- **Outcome:** Cardiogenic Shock Diagnosis
- **Exposure:** Biomarker of interest  
(per 1-SD, log-transformed)
- **Model:** Logistic regression

## Prognostic Outcomes Analysis

- **Outcome:** In-Hospital Mortality
- **Exposure:** Biomarker of interest  
(per 1-SD, log-transformed)
- **Model:** Logistic regression

**Adjusted for:** Age, sex, eGFR, HF, ACS, Cardiac Arrest

# Results

# Baseline Demographics

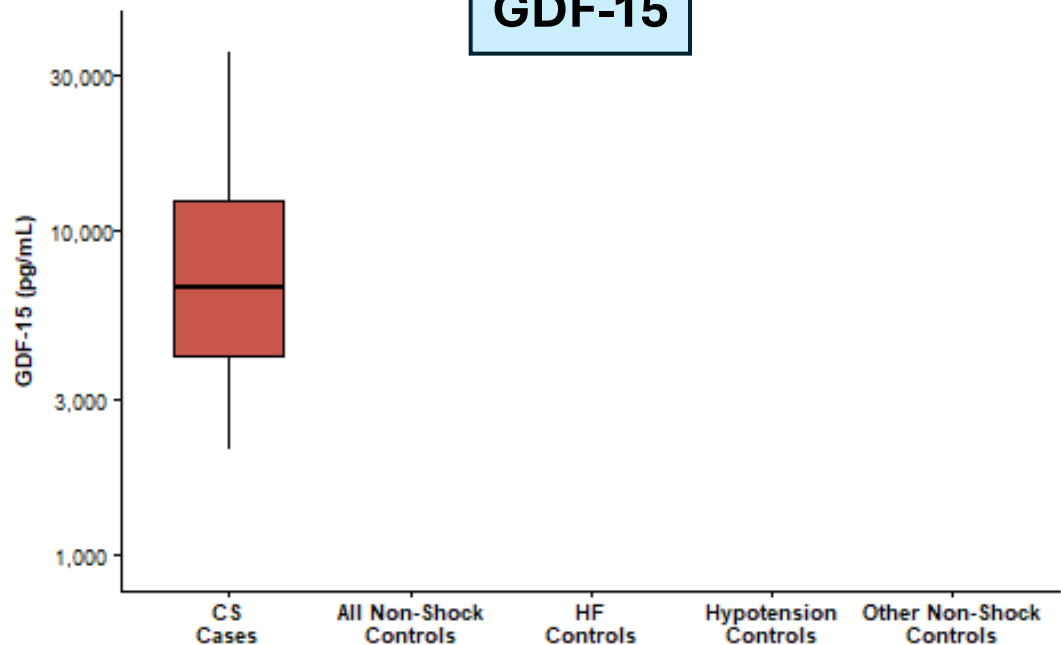
Characteristic	CS Cases (N=254)	All Non-Shock Controls (N=619)	Distributive Shock Cases (N=70)
<b>Demographics</b>			
Age, median (IQR), y	65 (54–74)	65 (55–74)	64 (56–72)
Female sex, No. (%)	33%	41%	24%
<b>Diagnosis</b>			
Acute coronary syndrome	28%	19%	7%
Heart failure	51%	26%	19%
Cardiac arrest	4%	2%	20%
<b>Clinical Variables</b>			
Mechanical support	48%	7%	7%
Renal replacement therapy	11%	3%	19%
<b>Laboratory Values</b>			
Baseline lactate, median (IQR)	2.1 (1.30-3.30)	1.40 (1.1-2.0)	2.00 (1.2-4.5)
Baseline eGFR, median (IQR)	43 (29-64)	68 (48-88)	45 (28-66)

# Baseline Demographics

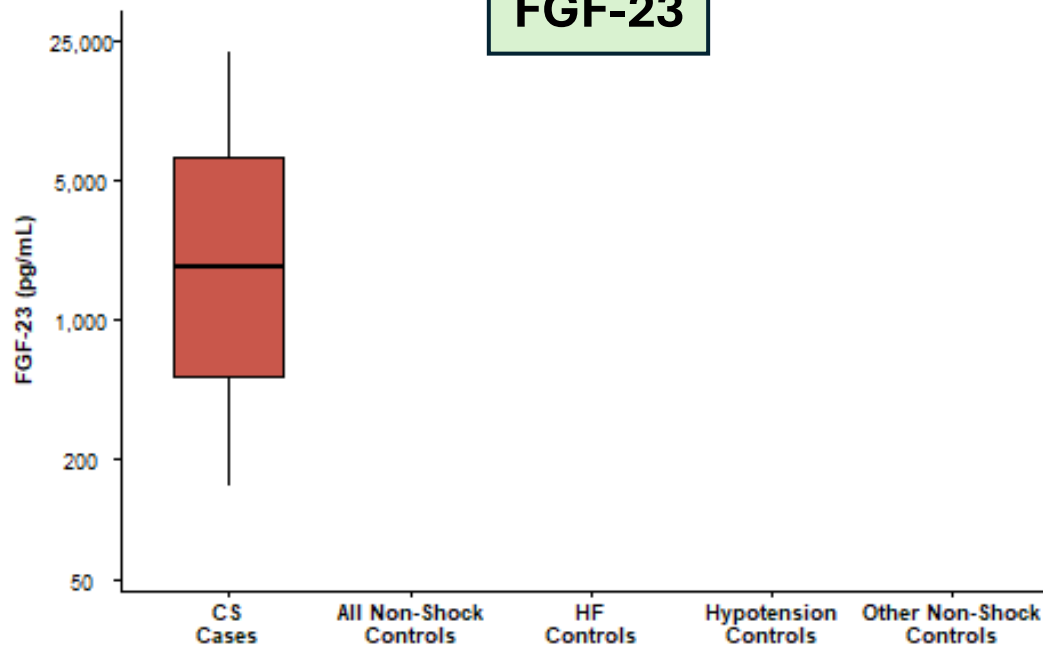
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# Biomarker Distributions

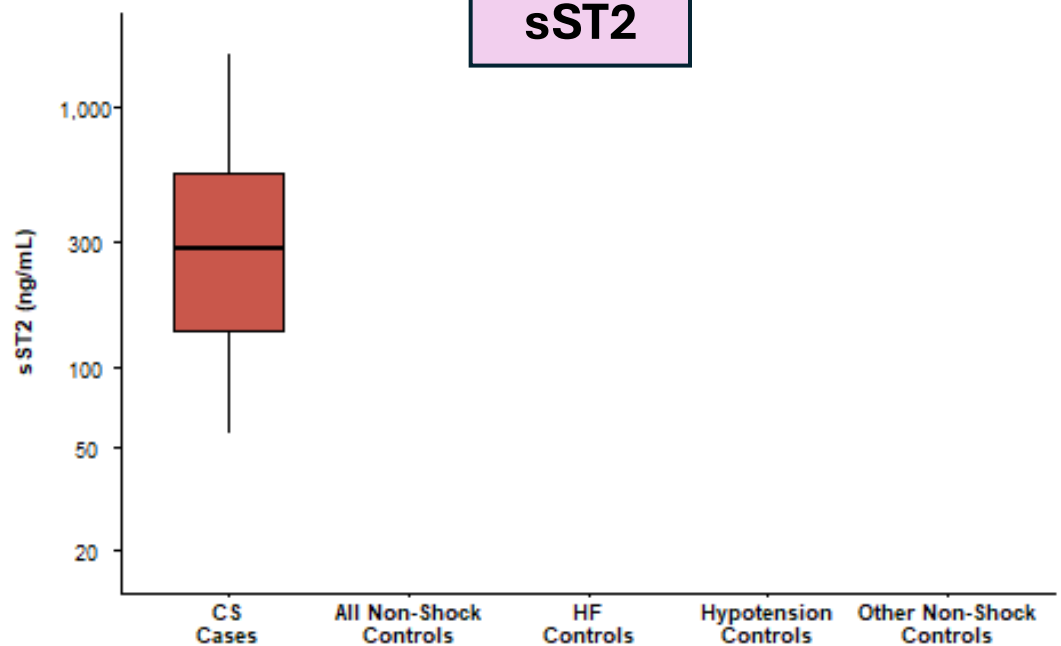
### GDF-15



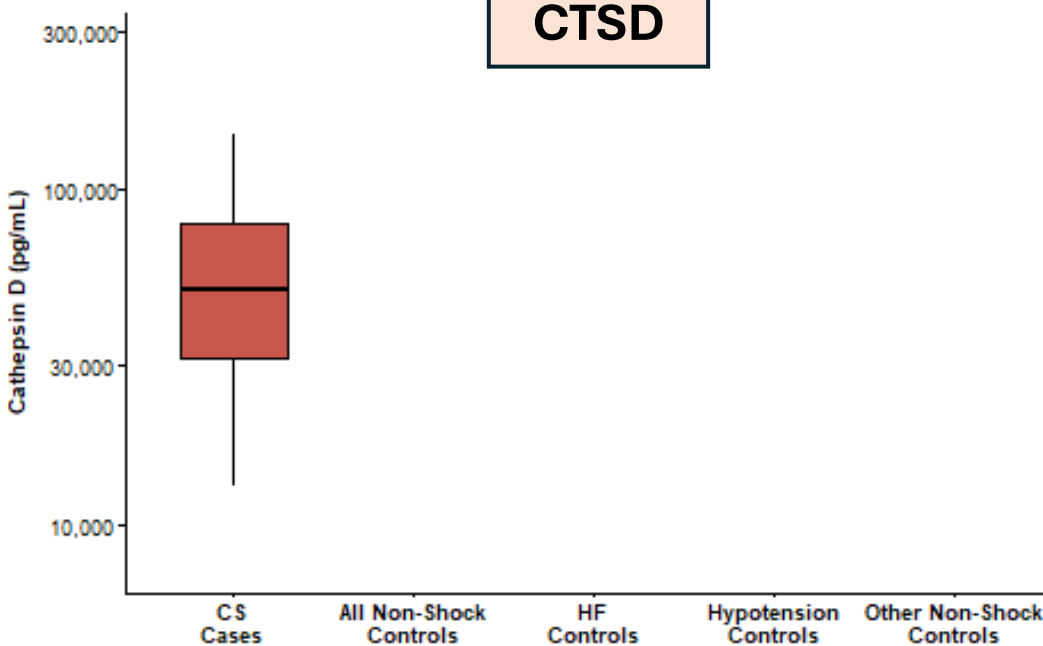
### FGF-23



### sST2

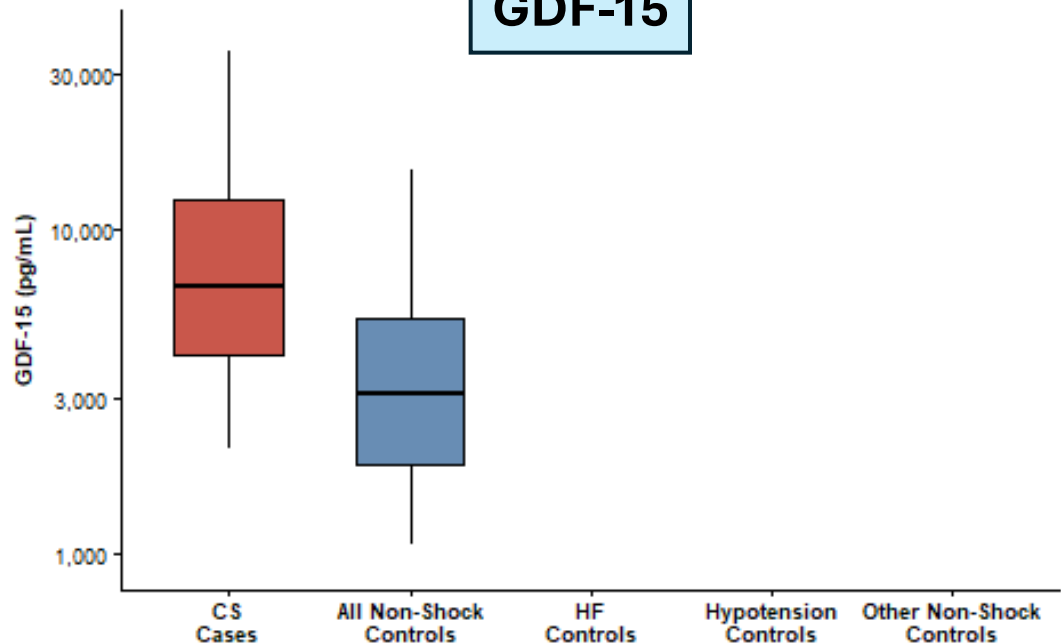


### CTSD

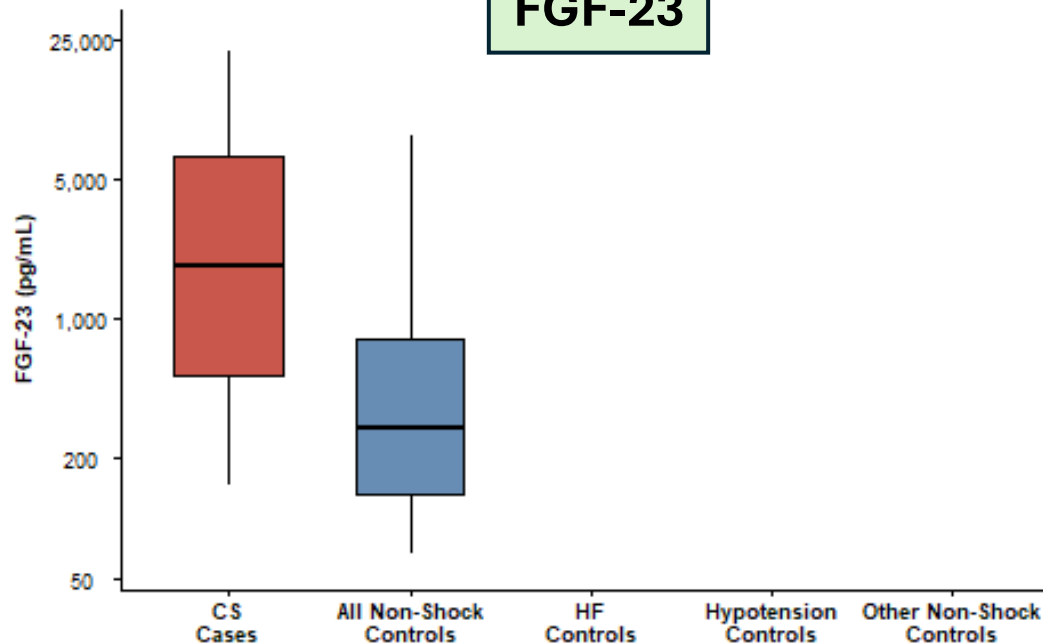


**Box:** IQR (25th–75th percentile);  
**Line:** median;  
**Whiskers:** 5th–95th percentiles.

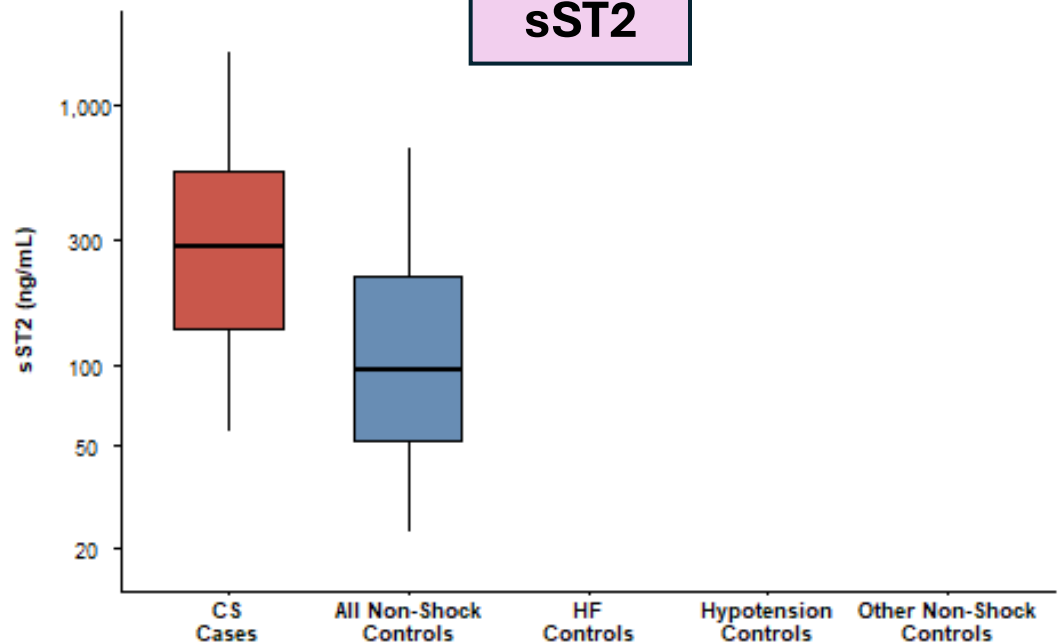
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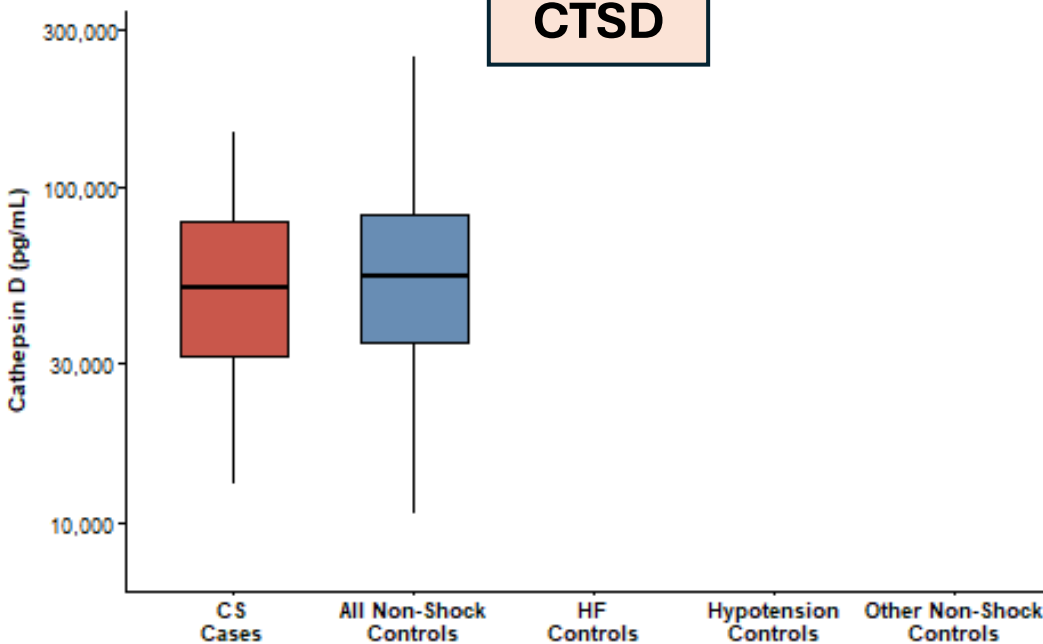
### FGF-23



### sST2

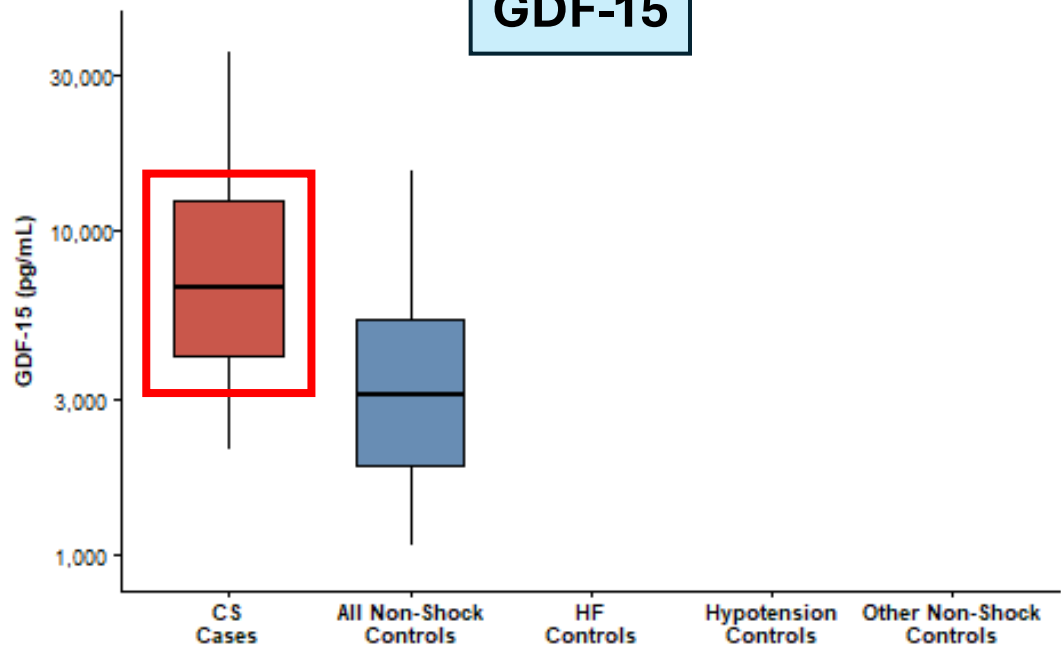


### CTSD

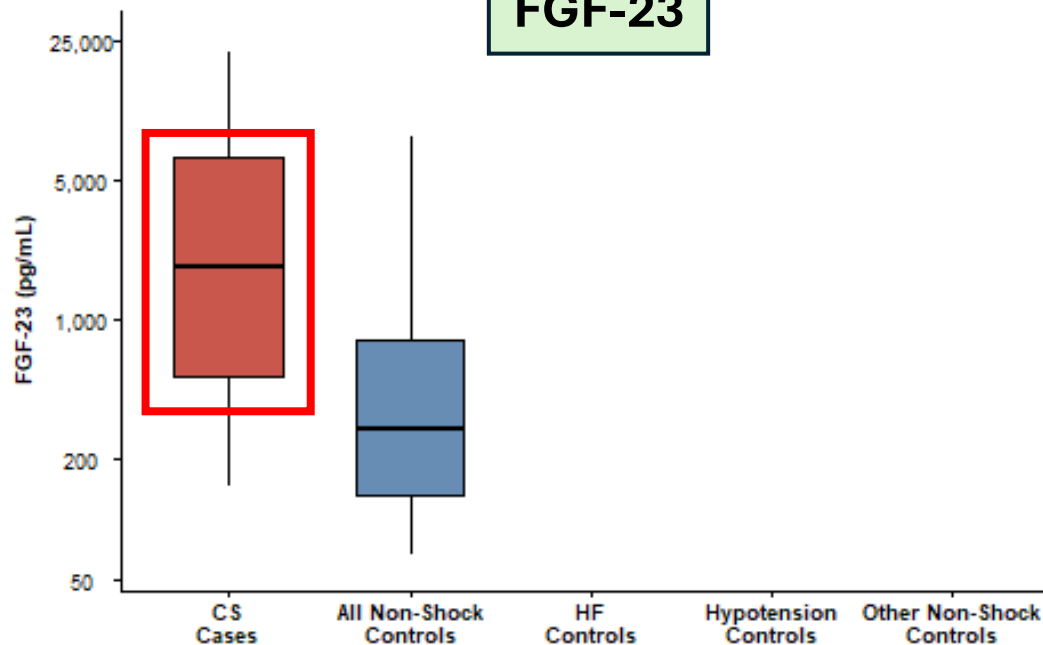


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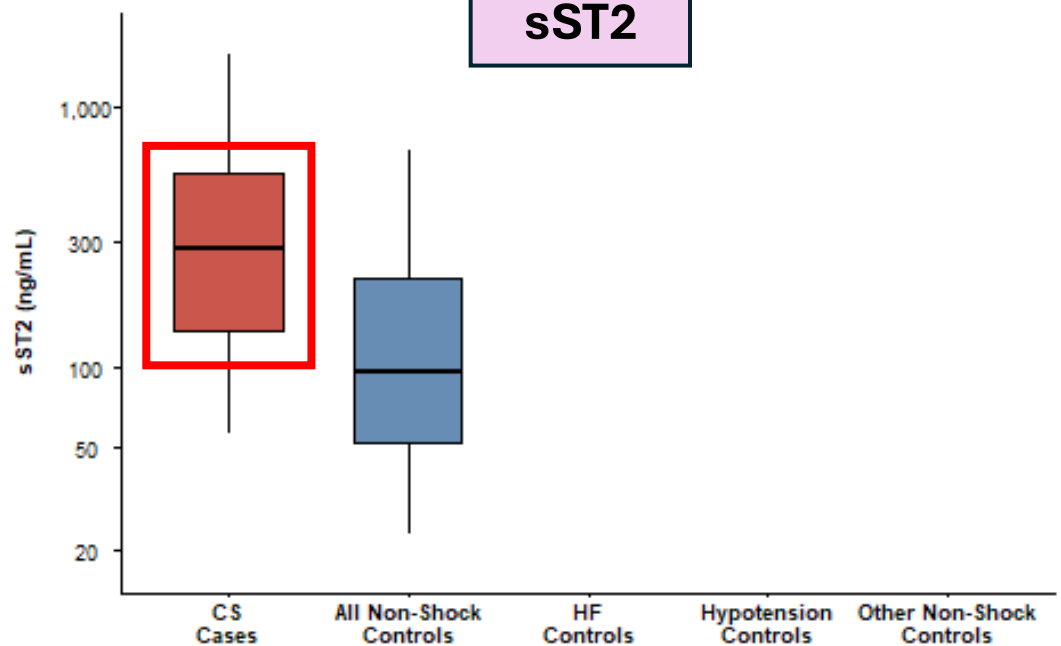
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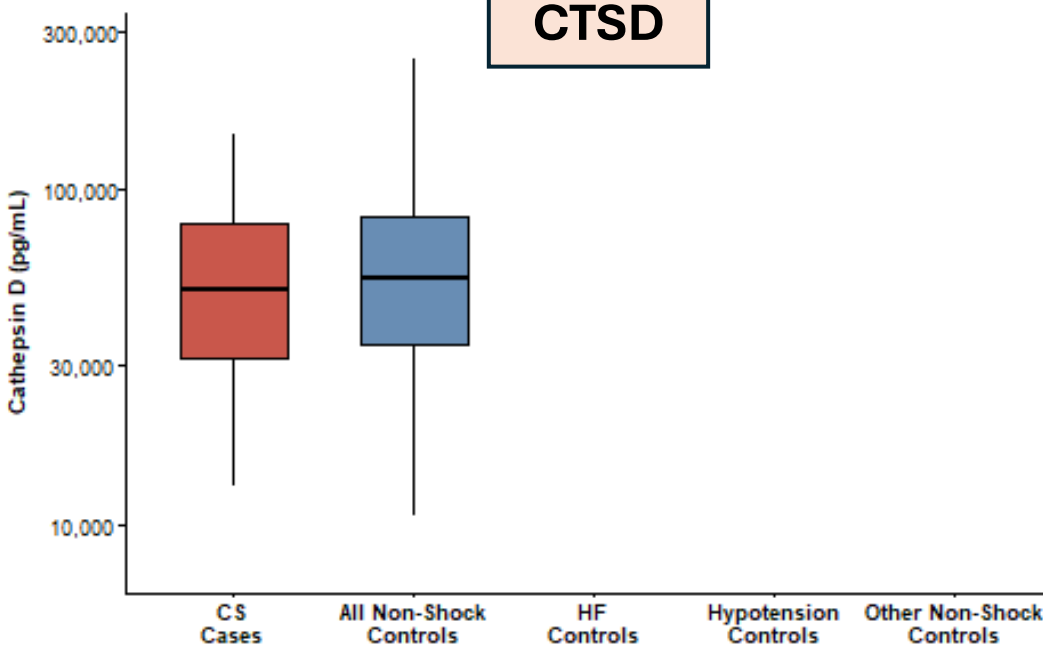
### FGF-23



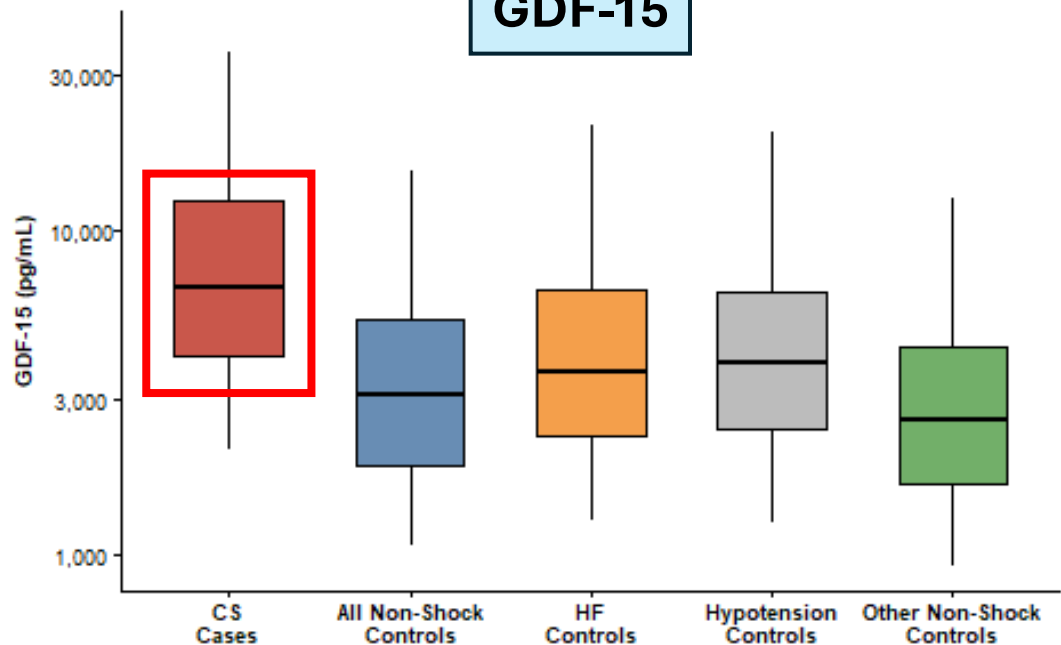
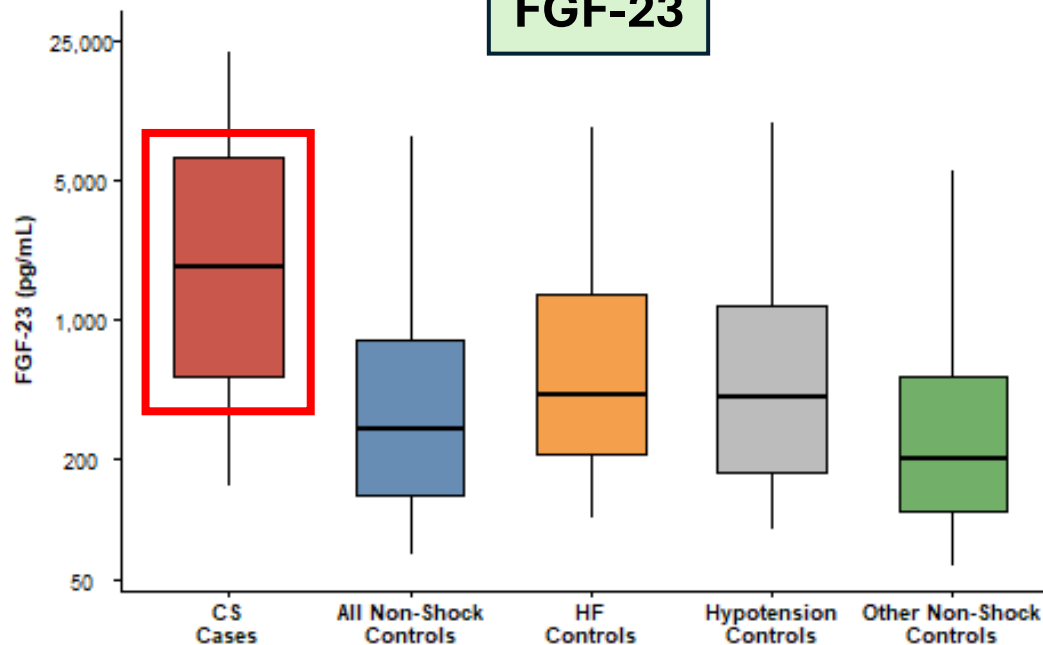
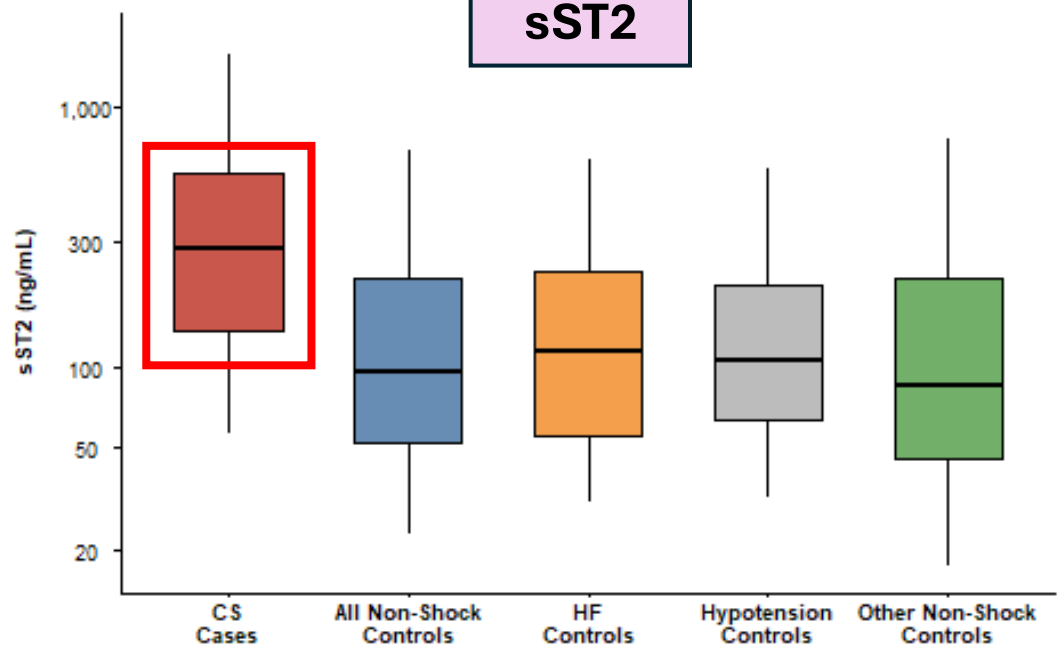
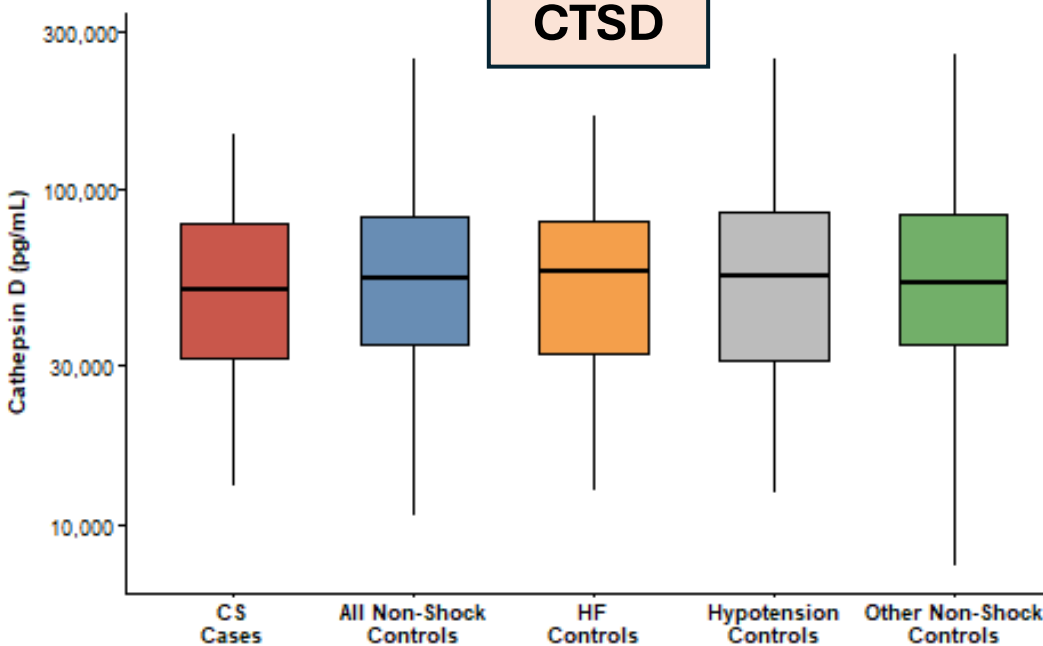
### sST2



### CTSD

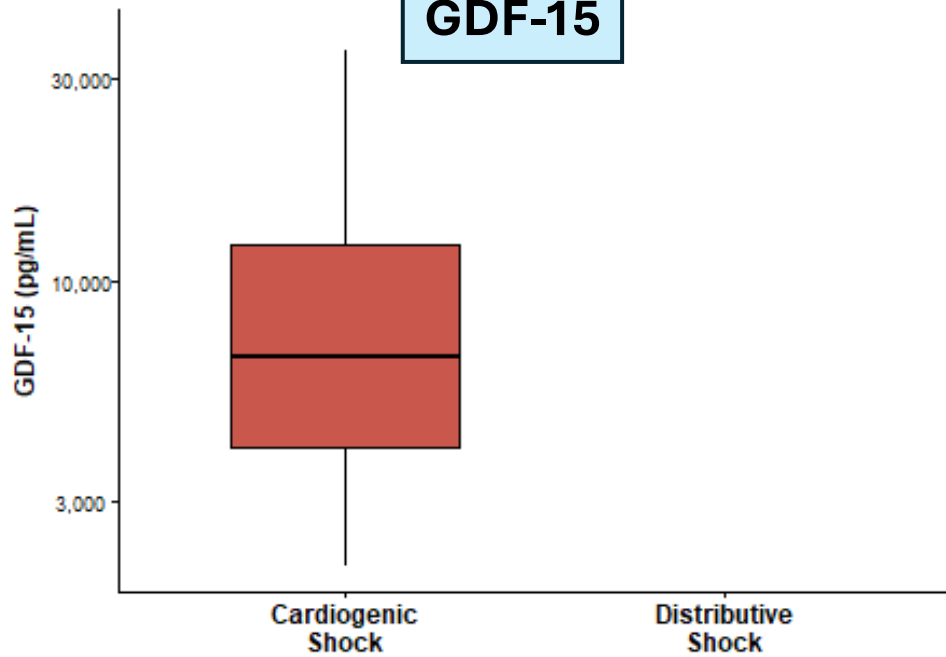


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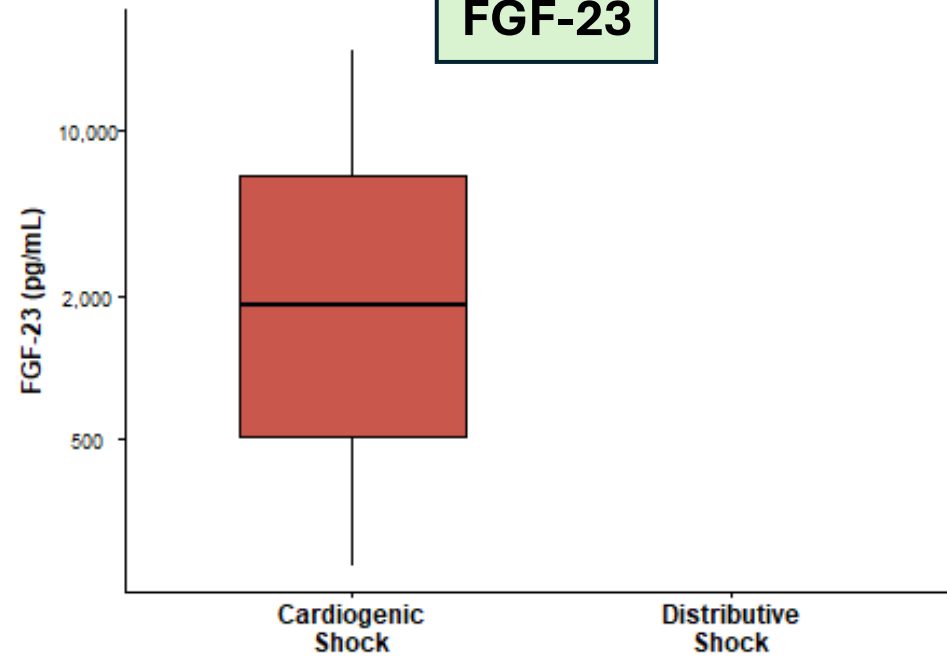
**GDF-15****FGF-23****sST2****CTSD**

**Box:** IQR (25th–75th percentile);  
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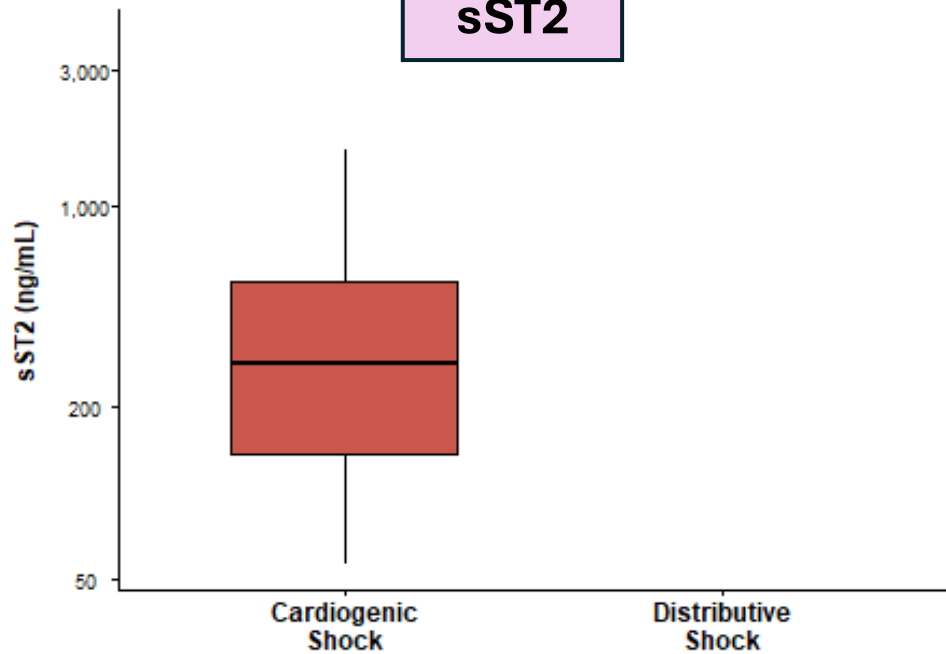
**GDF-15**



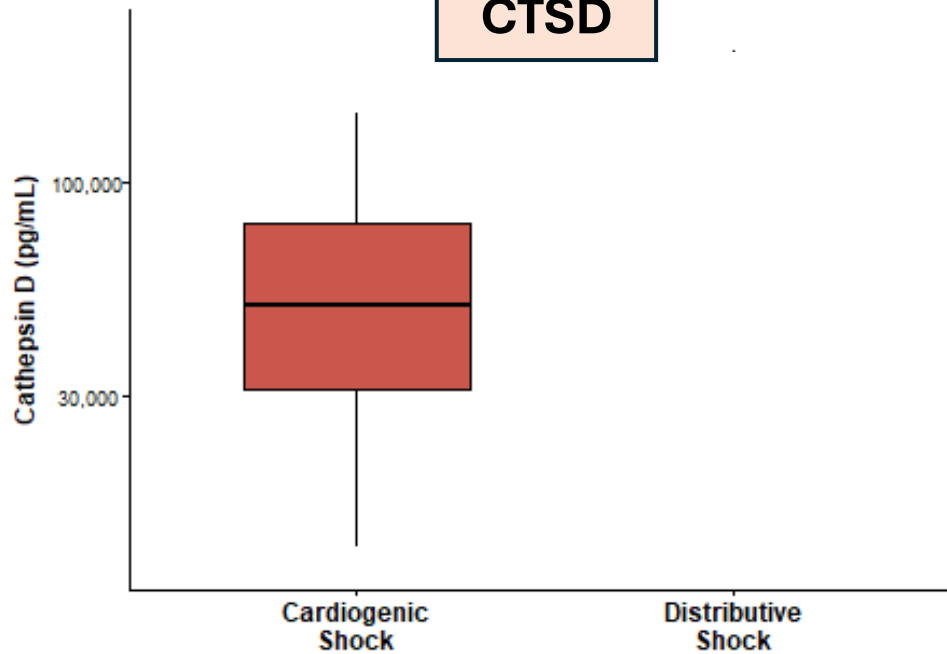
**FGF-23**



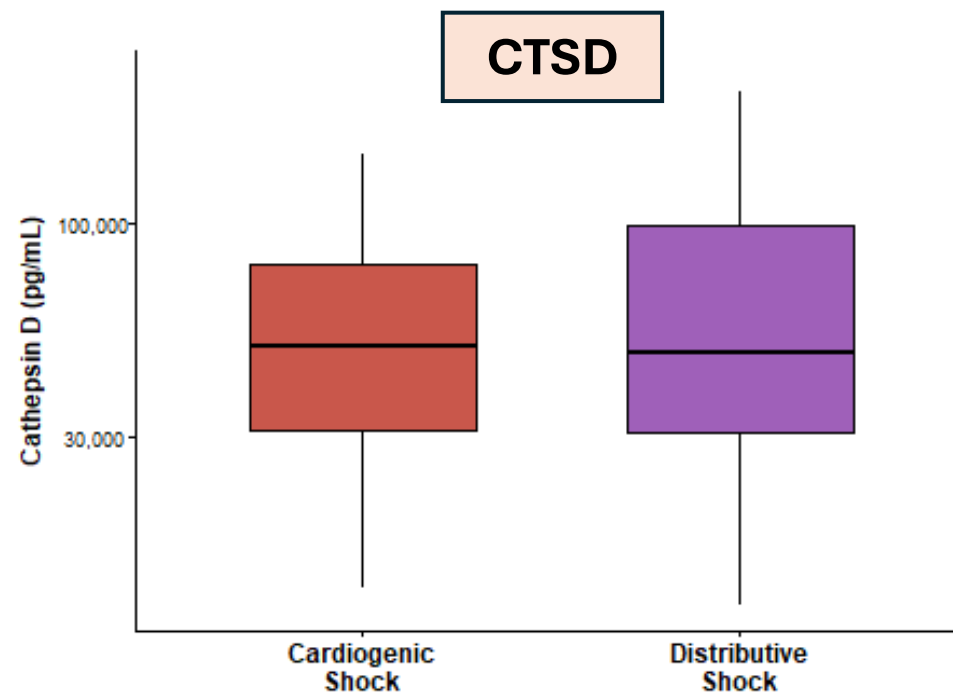
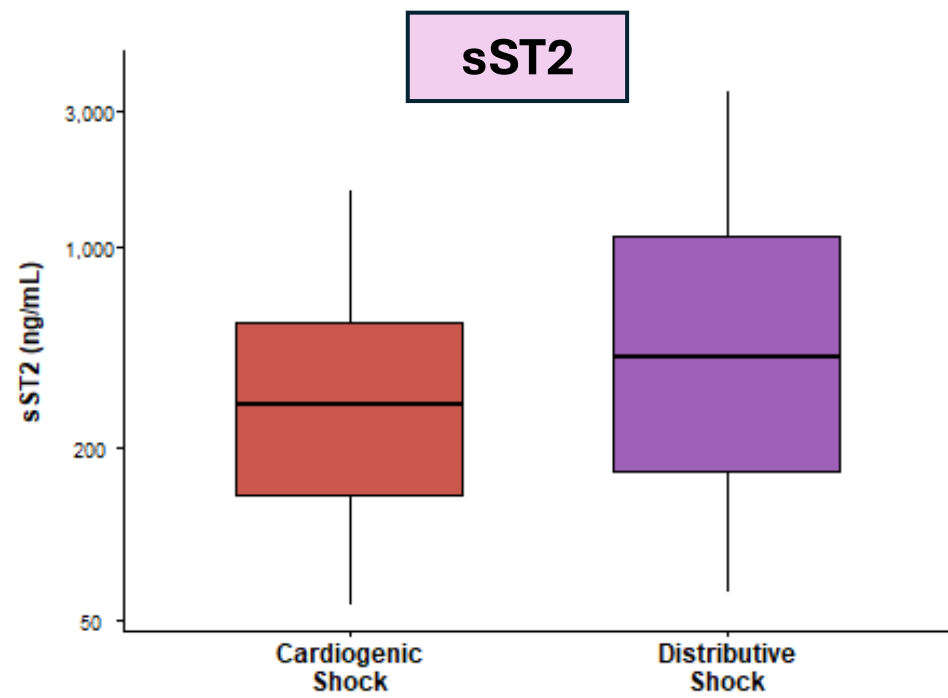
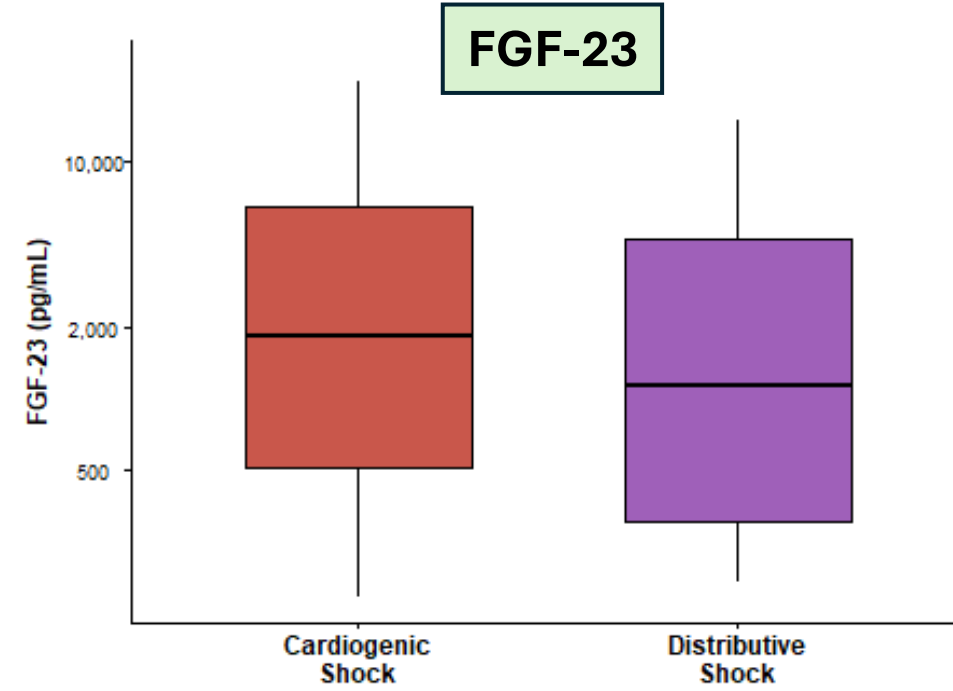
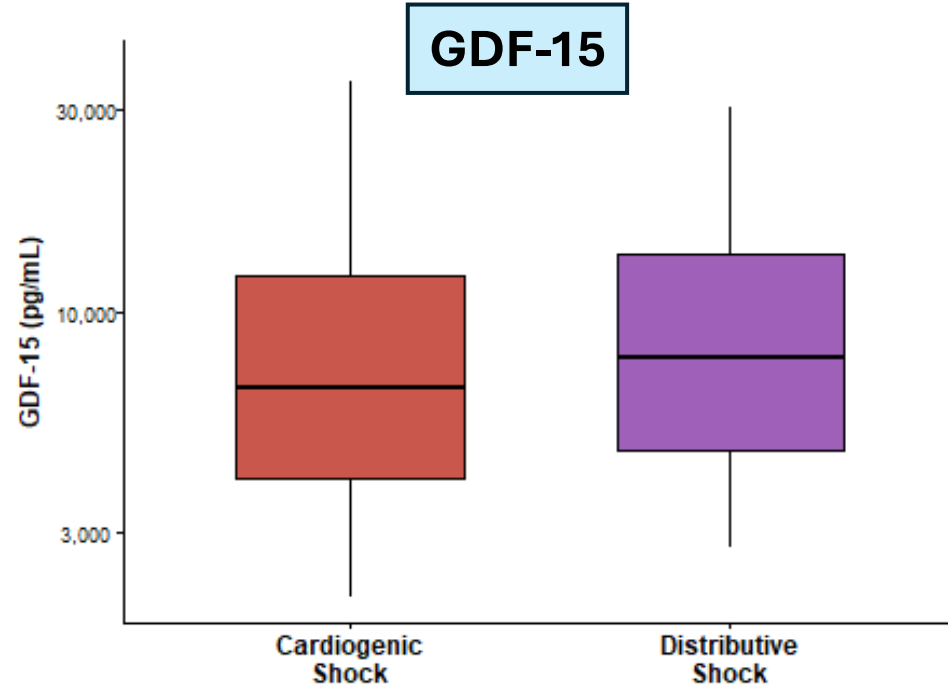
**sST2**



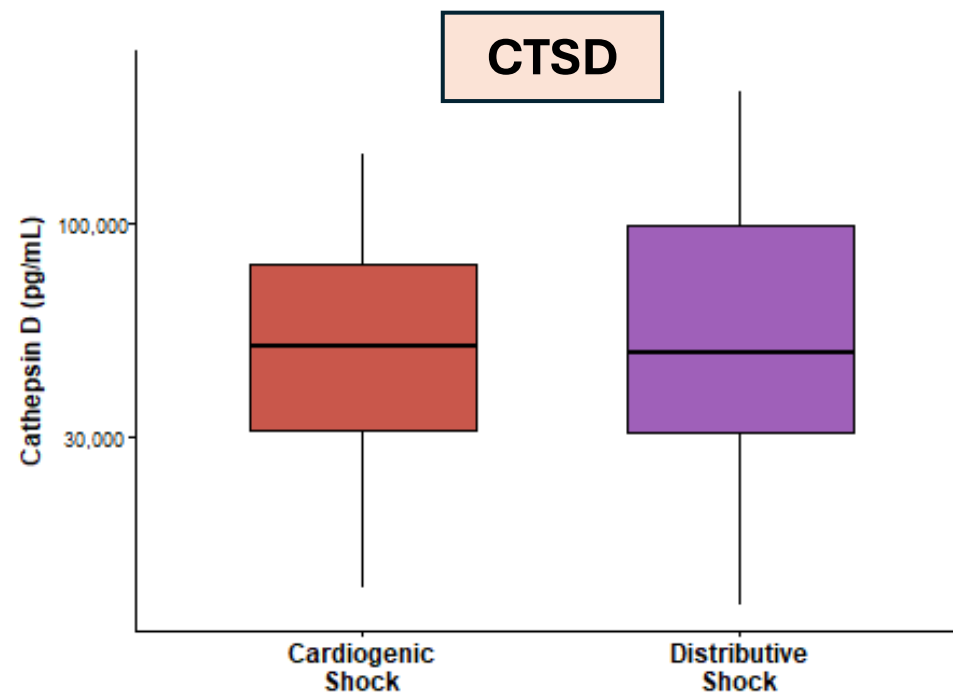
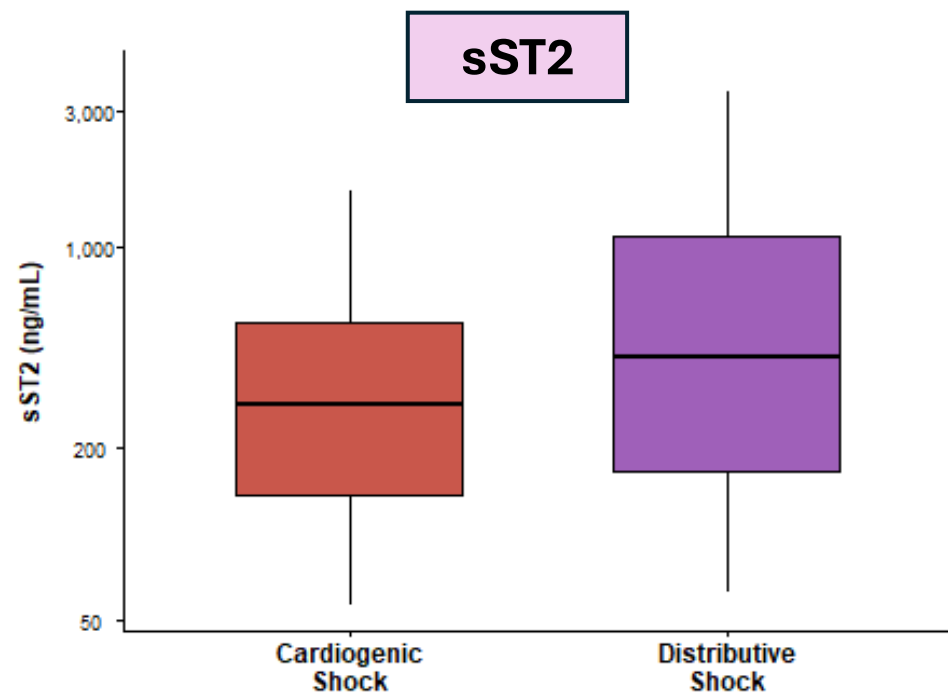
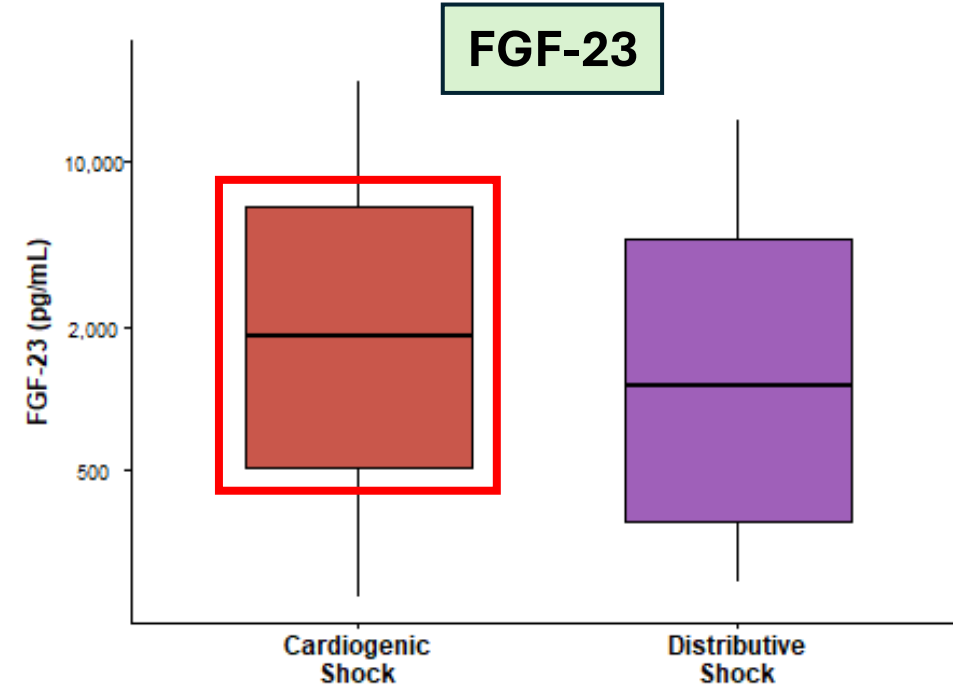
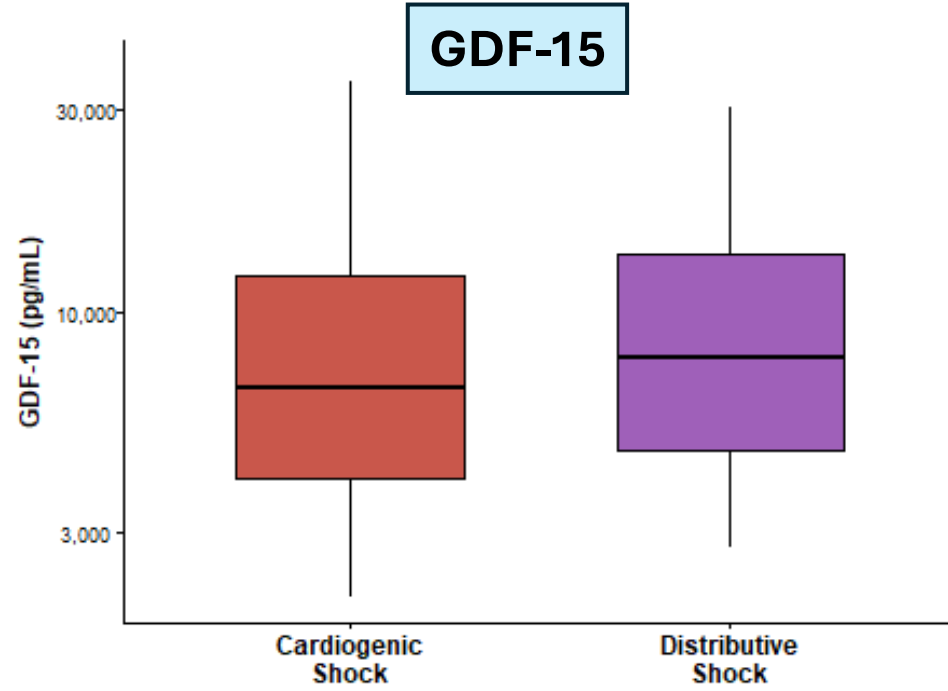
**CTSD**



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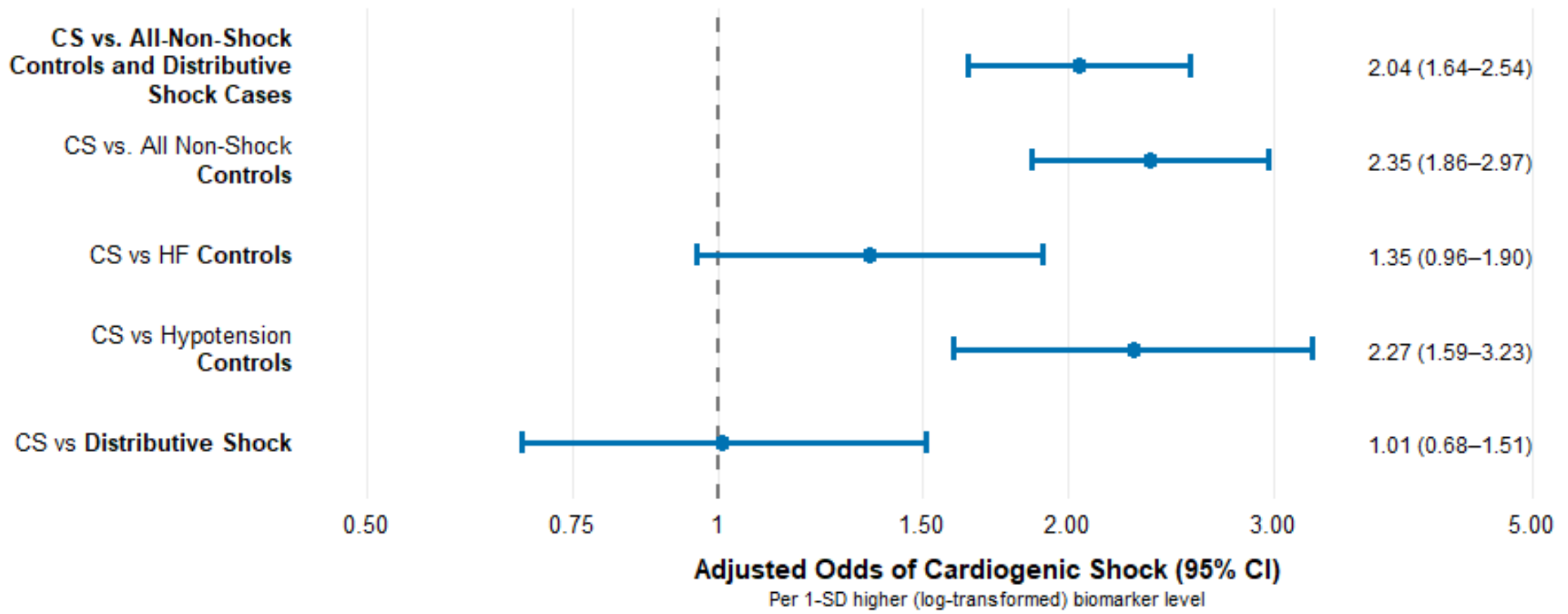
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# Diagnostic Performance

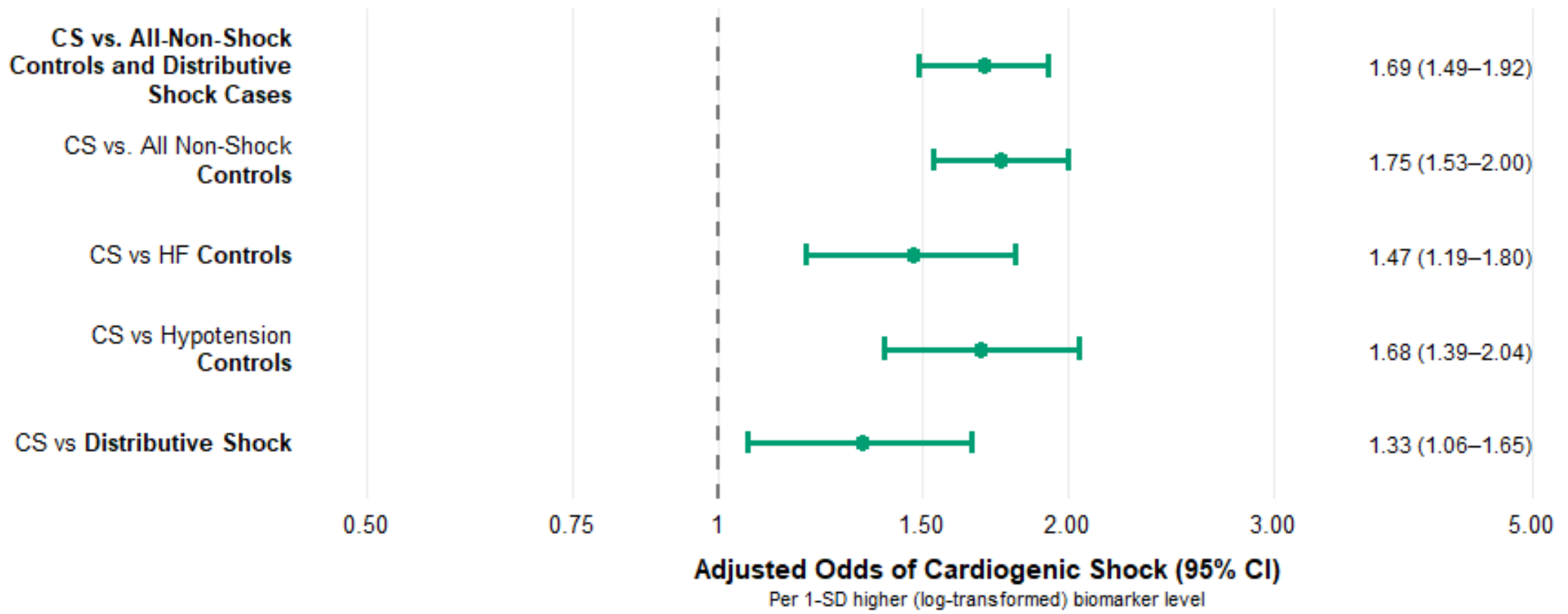
## GDF-15



Adjusted for: Age, sex, eGFR, HF, ACS, Cardiac Arrest

# Diagnostic Performance

## FGF-23

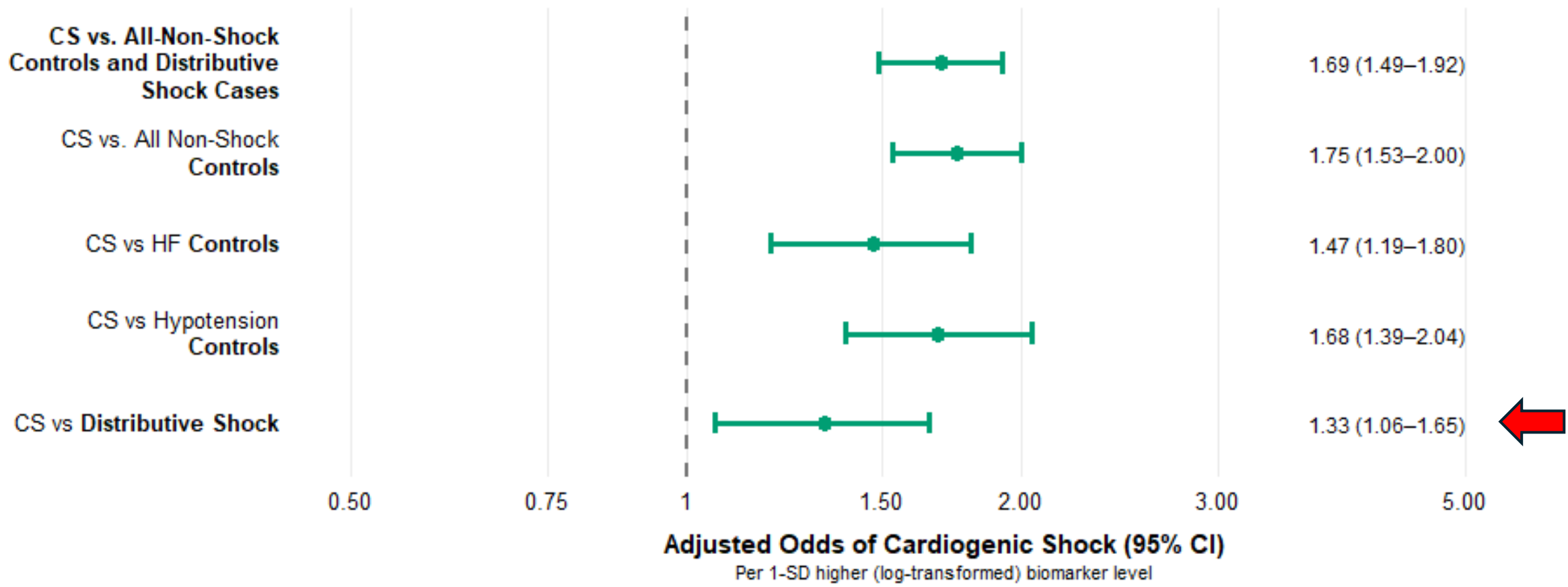


Adjusted for: Age, sex, eGFR, HF, ACS, Cardiac Arrest



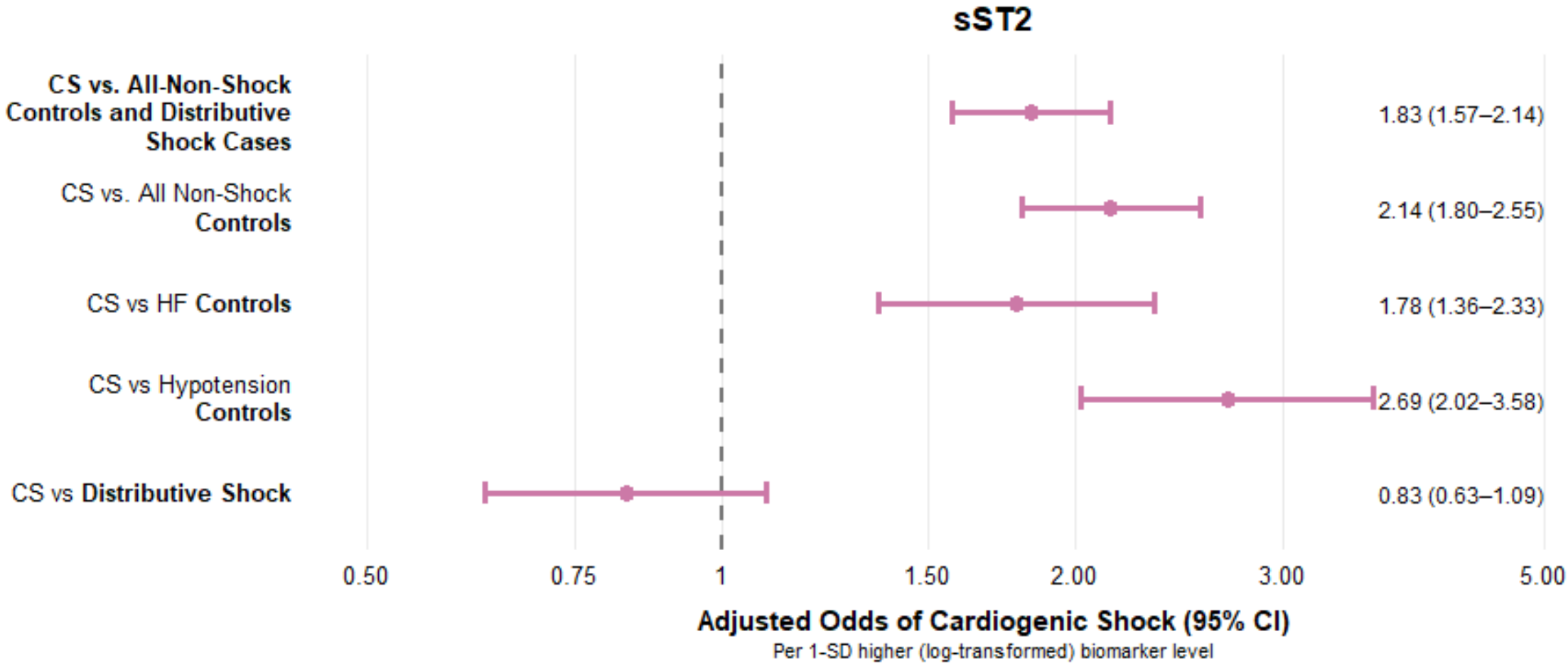
# Diagnostic Performance

## FGF-23



Adjusted for: Age, sex, eGFR, HF, ACS, Cardiac Arrest

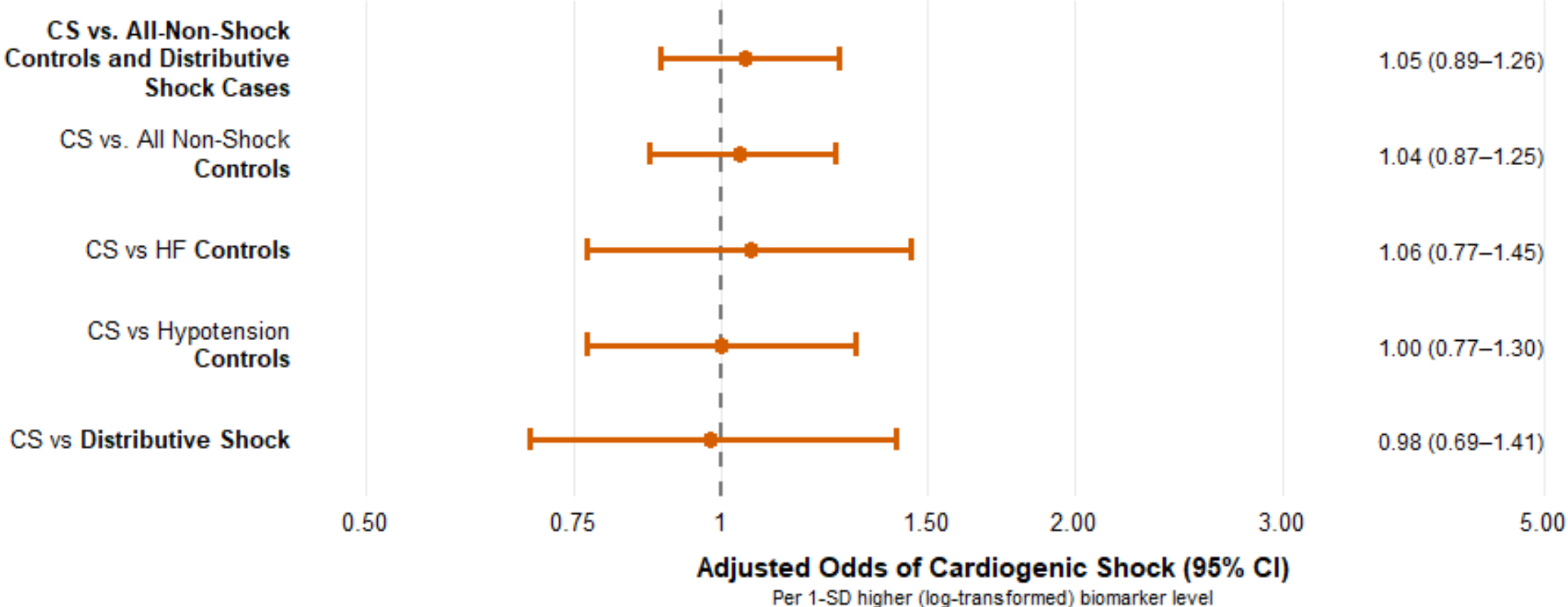
# Diagnostic Performance



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# Diagnostic Performance

CTSD

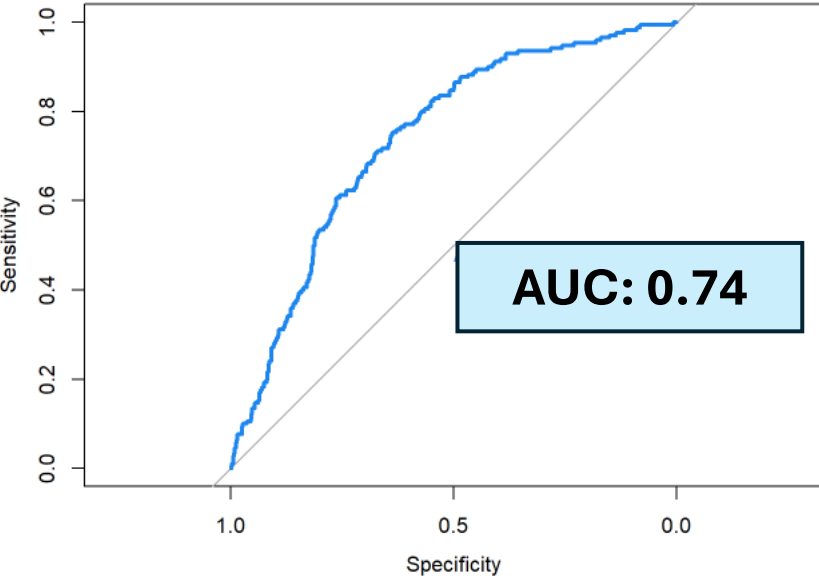


Adjusted for: Age, sex, eGFR, HF, ACS, Cardiac Arrest

# ROC Curves for Diagnostic Performance

# Optimal Lab Thresholds for Predicting Cardiogenic Shock Diagnosis

**GDF-15**

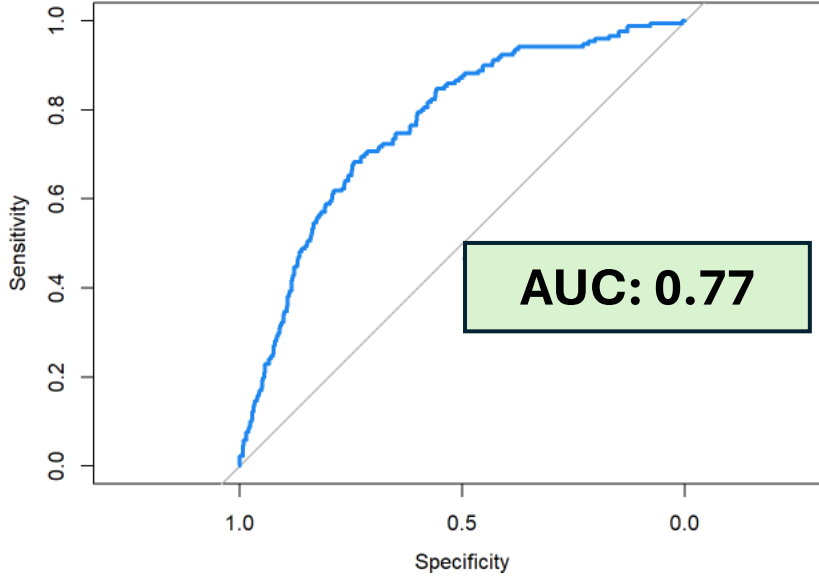


**AUC: 0.74**

**Optimal threshold: 3983 pg/mL**  
(Ref Range: 399–866 ng/L)

**PPV: 34%**  
**NPV: 91%**

**FGF-23**

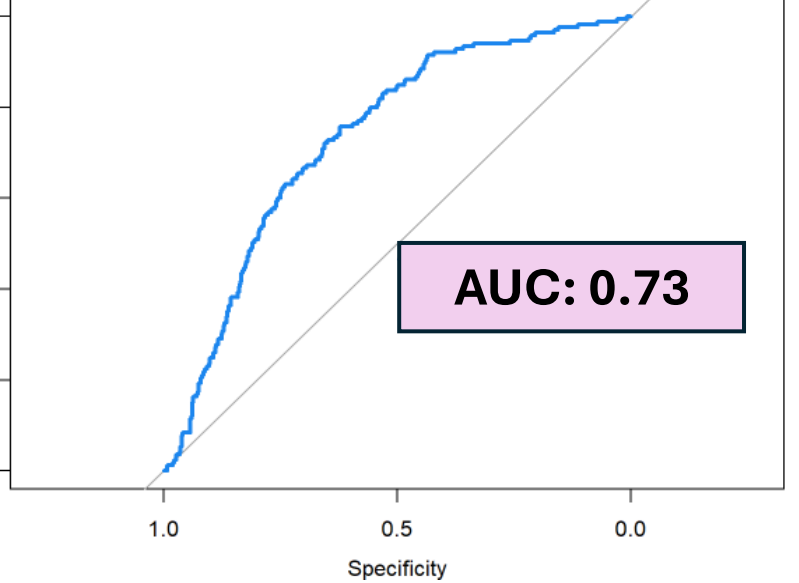


**AUC: 0.77**

**Optimal threshold: 519 pg/mL**  
(Ref Range: 16.1–49.3 pg/mL)

**PPV: 40%**  
**NPV: 90%**

**sST2**



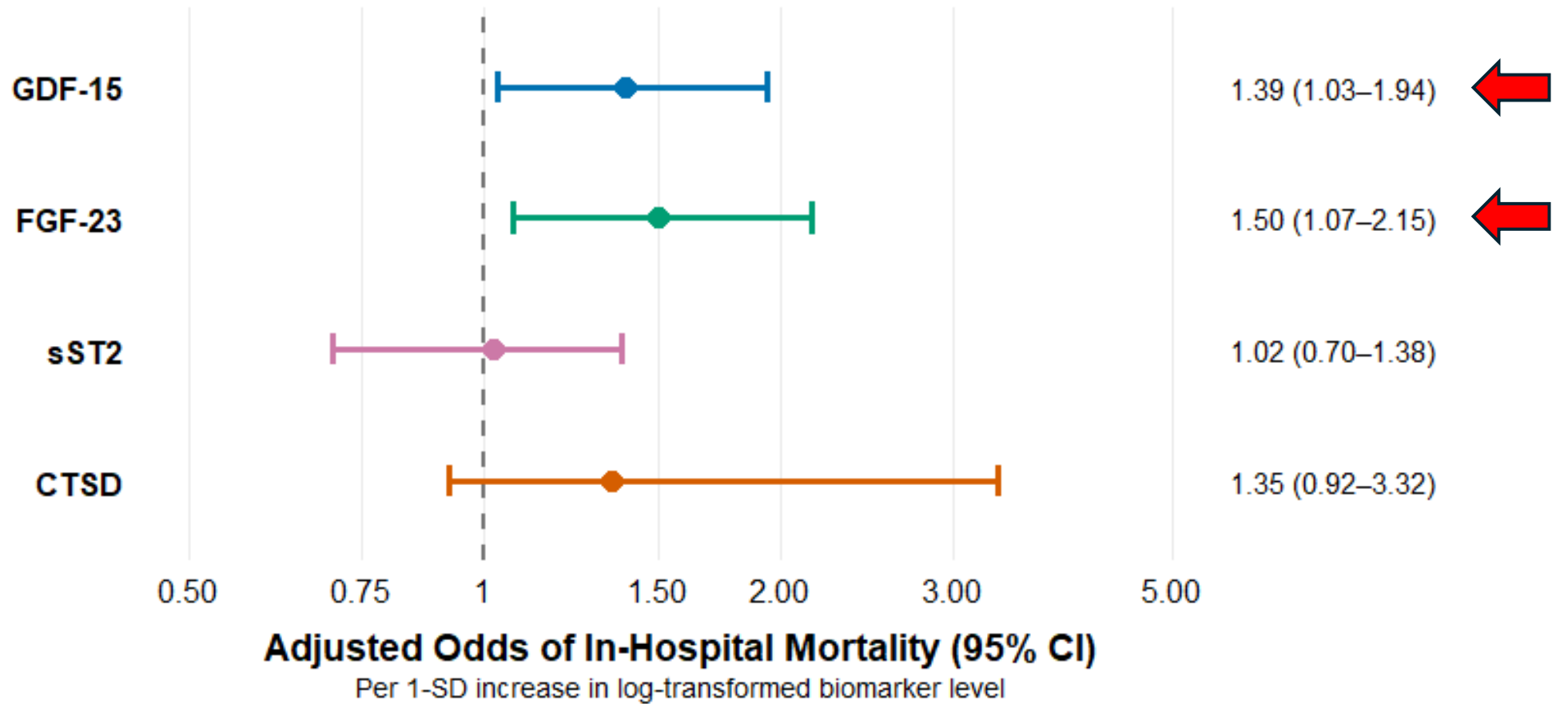
**AUC: 0.73**

**Optimal threshold: 137 ng/mL**  
(Ref Range: 8.6–49.3 ng/mL)

**PPV: 33%**  
**NPV: 91%**

# Prognostic Performance (Mortality)

# Mortality Amongst CS Cases



Adjusted for: Age, sex, eGFR, HF, ACS, Cardiac Arrest

# Conclusions & Implications

**FGF-23**, **GDF-15**, and **sST2** demonstrated **strong *diagnostic discrimination*** for **cardiogenic shock** vs. **non-shock controls**

**FGF-23** showed potential ***diagnostic discrimination*** for **CS** vs. **distributive shock**.

**FGF-23** and **GDF-15** were independently associated with ***in-hospital mortality*** suggesting **prognostic utility** beyond diagnosis.

# Thank You!

- Kyle M. Gibson MD MS
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- Michael Miller MD
- Siddharth M. Patel MD MPH
- Sachit Singal MD
- Andre M. Small MD
- Sepahrad Zamani MD
- Erin A. Bohula MD DPhil



**David Berg, MD, MPH**



**David Morrow, MD, MPH**