



# Autonomic nervous system function in Long-COVID: prevalence of cardiovascular autonomic abnormalities and sex-based differences

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## Background:

### Long-COVID

- Patients left with a **constellation of symptoms >3 months** after resolution of the acute illness
- Symptoms: fatigue, light-headedness, or tachycardia, relieved only by recumbence

### Some meet hemodynamic criteria for autonomic abnormalities:

- Postural Orthostatic Tachycardia Syndrome (POTS)
- Initial Orthostatic Hypotension (IOH)
- Orthostatic Hypotension (OH)
- Inappropriate Sinus Tachycardia (IST)

The prevalence of autonomic abnormalities and sex-based differences in Long-COVID are **unknown**

## Research Questions:

What is the prevalence of autonomic abnormalities, and is there a sex-difference among patients with Long-COVID?

## Methods:

**10 min supine baseline** followed by a **10 min active stand**

- Beat-to-beat hemodynamics
- Evaluation of autonomic abnormalities
  - POTS ( $\Delta HR \geq 30 \text{ bpm}$  within 10min)
  - IOH (transient  $\Delta SBP \geq -40 \text{ mmHg}$  within 15s)
  - OH ( $\Delta SBP \geq -20 \text{ mmHg}$  within 3min)
  - IST (supine HR  $> 100 \text{ bpm}$ )

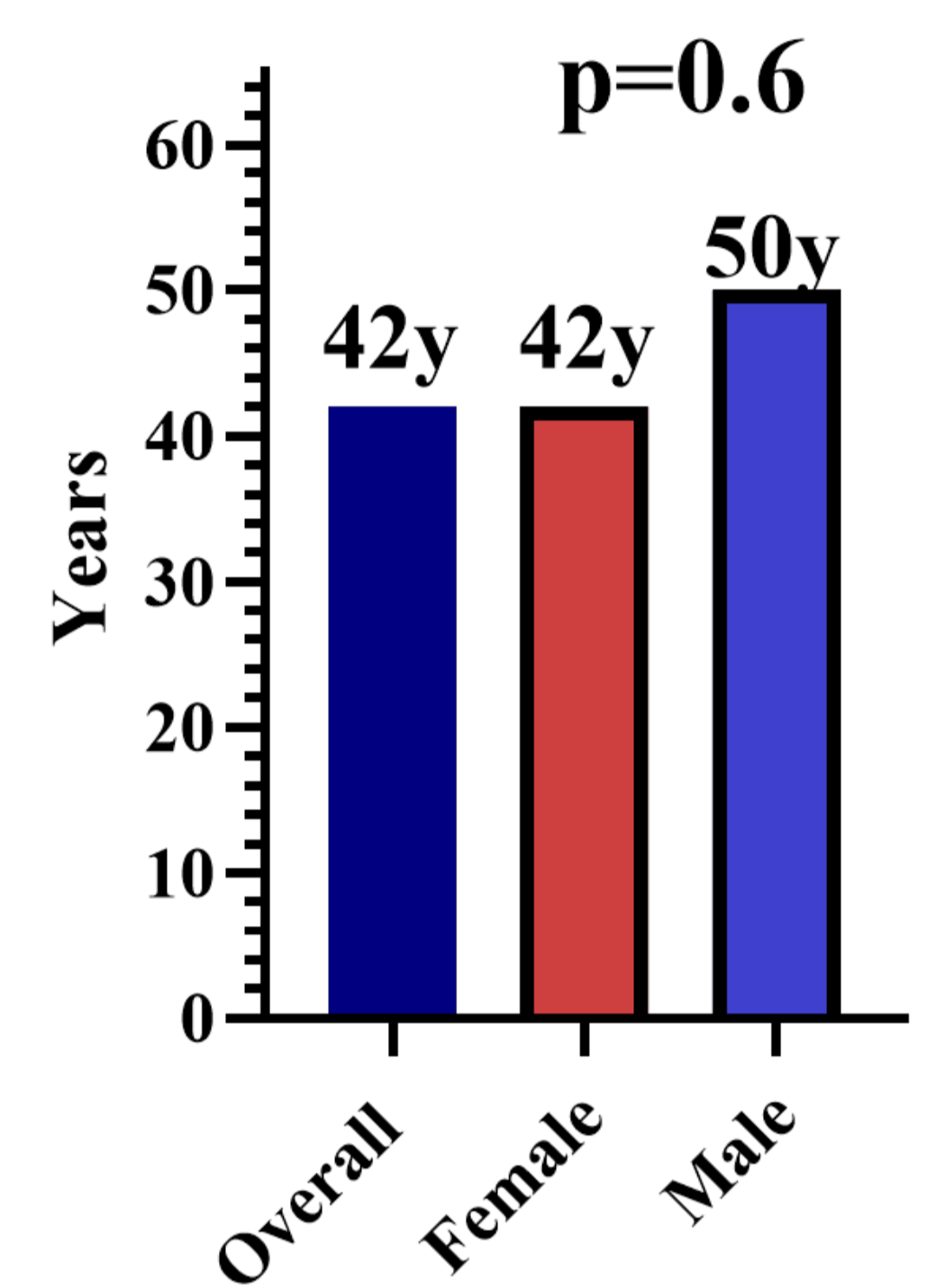
## Statistical Analyses:

- Categorical data were analyzed with a **Fischer's Exact test**

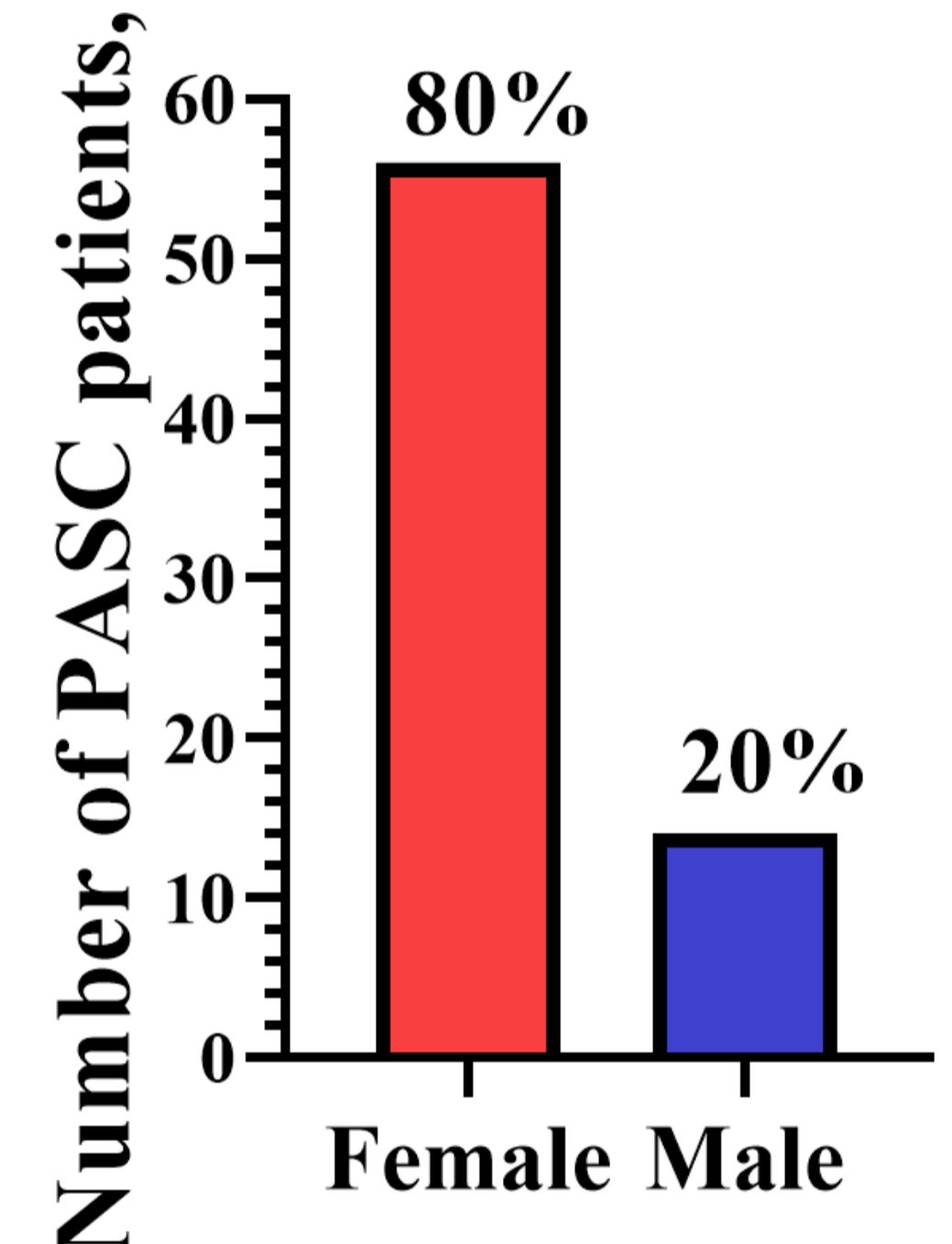
## Results –

### Demographics: n = 70 Patients with Long-COVID

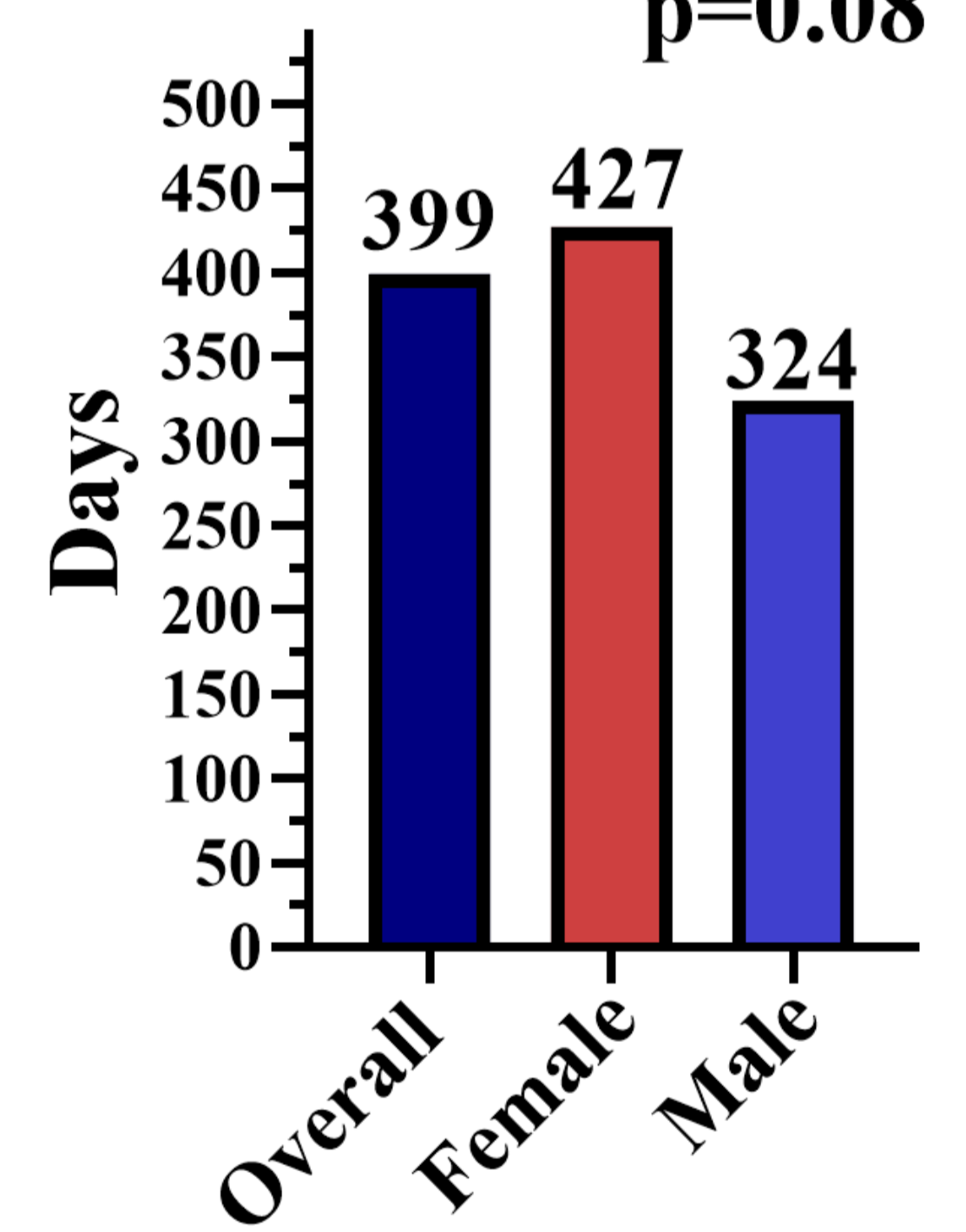
#### Age



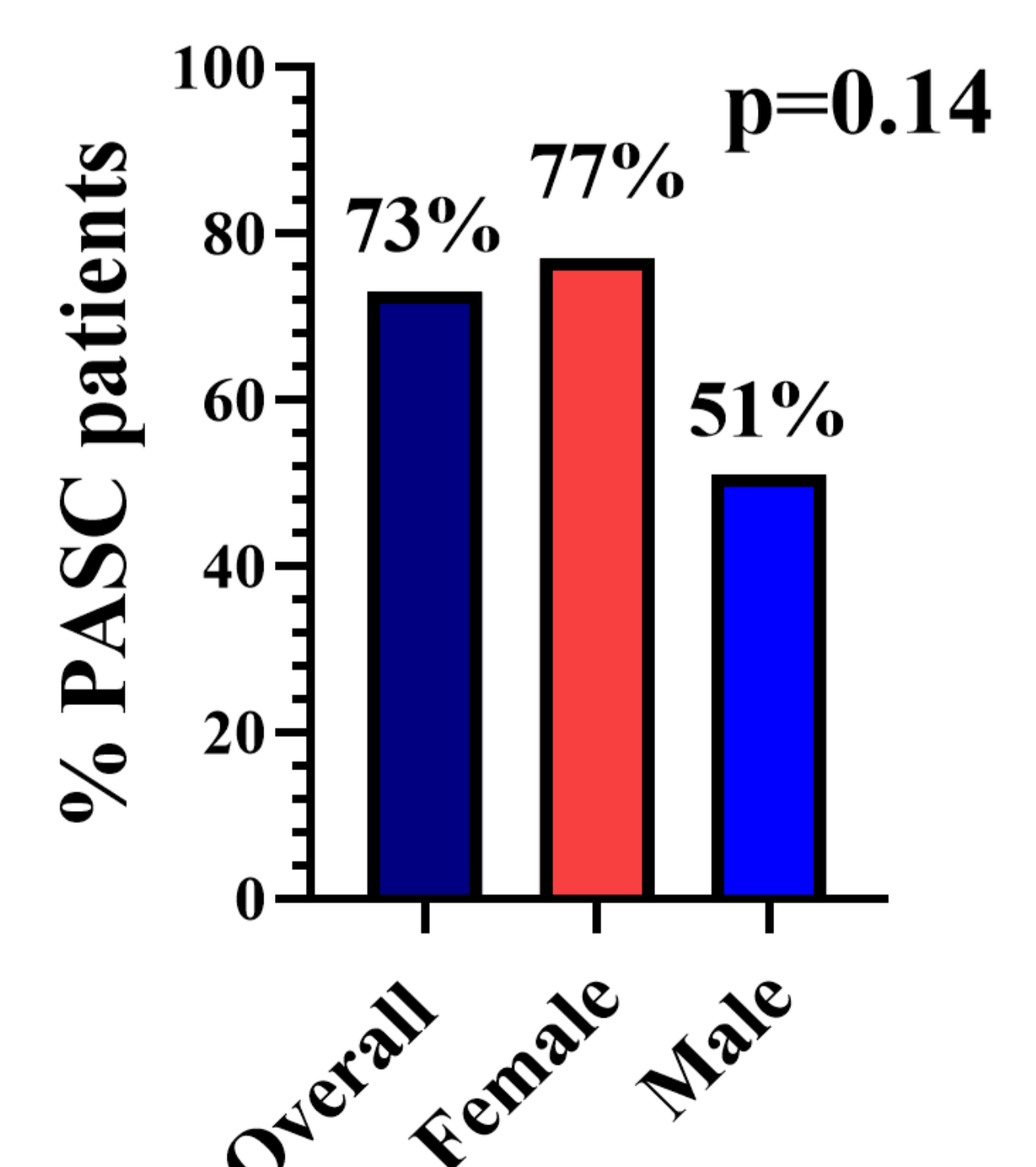
#### Sex



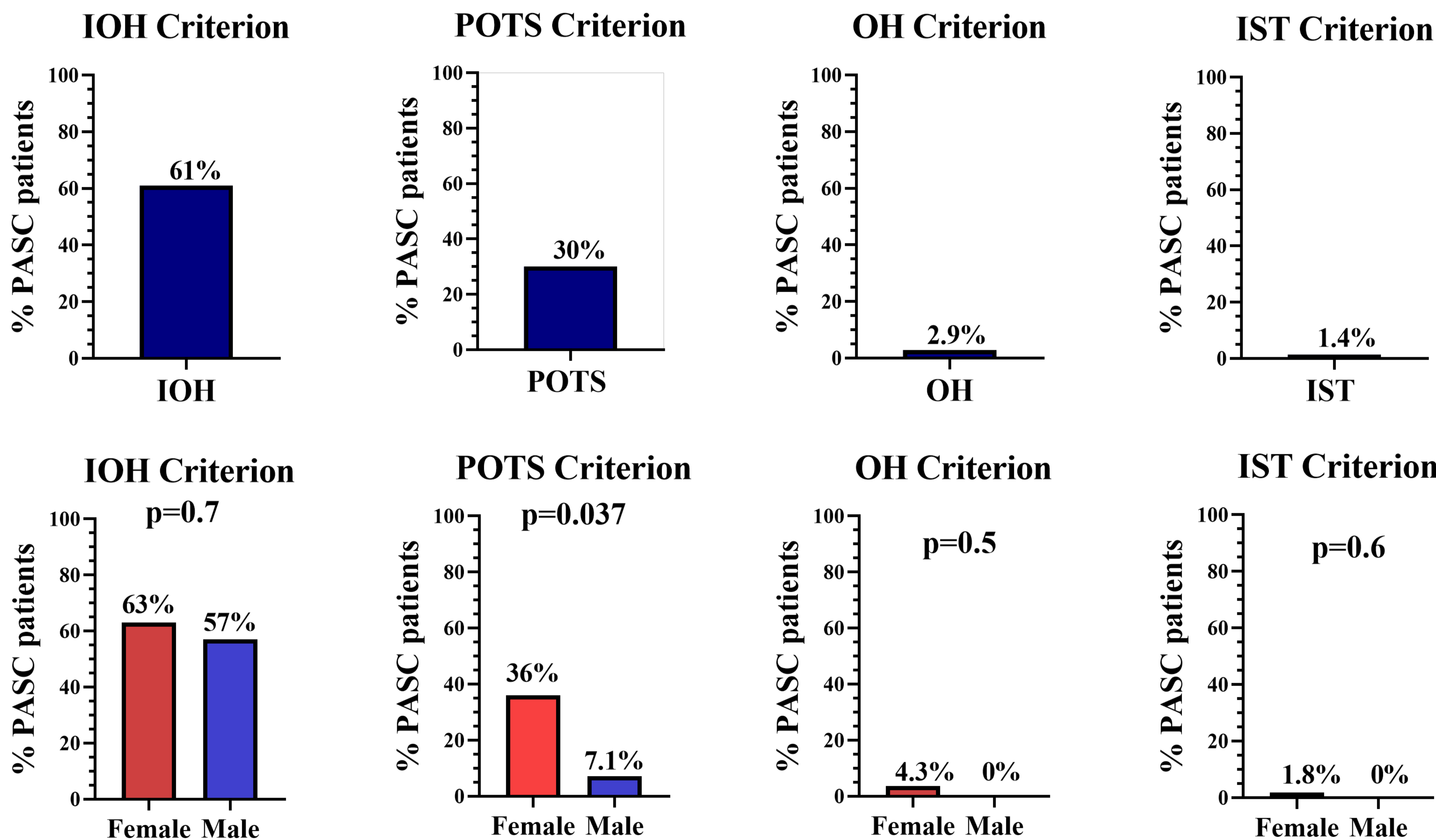
### COVID Duration p=0.08



### Overall Prevalence of Abnormalities



## Results – Overall Prevalence and Sex-Based Differences:



## Conclusions:

- Patients with Long-COVID have **evidence** of autonomic cardiovascular **abnormalities**
- IOH most common and will be missed unless an **active stand** protocol used
- POTS is more common in **females**, but IOH was **equally evident** between sexes

## Equity, Diversity, and Inclusion (EDI) & Sex- and Gender-Based Analysis+ (SGBA+) Integration/Considerations

- This study is not limited to any one race, gender, or sexual orientation. It is open to anyone who wishes to participate. This will improve the generalizability and include patients of different backgrounds. The research team is composed of patient partners and researchers to ensure the study protocol is centered around patient-identified outcomes.
- We have conducted disaggregated analyses of primary and secondary outcome measures based on sex and will conduct stratified analyses based on self-described gender.

## Keywords:

- COVID-19; Autonomic; Dysfunction; Long-COVID



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**BACKGROUND:** Many patients are left with symptoms several months after resolution of the acute COVID-19 infection (“Long-COVID”), including fatigue, light-headedness, and tachycardia/palpitations. These resemble cardiovascular autonomic disorders such as Postural Orthostatic Tachycardia Syndrome (POTS), Initial Orthostatic Hypotension (IOH), Orthostatic Hypotension (OH), and Inappropriate Sinus Tachycardia (IST). Currently, we do not know the prevalence of autonomic abnormalities in Long-COVID patients, nor if there are sex-differences. We aimed to determine the prevalence of autonomic abnormalities, and whether there was a sex-difference among Long-COVID patients.

**METHODS:** Long-COVID patients (n=70; F=56; 42±11y) underwent a 10-minute supine baseline followed by a 10-minute active stand with beat-to-beat hemodynamics 399±129 days after their COVID-19 infection. Patients were evaluated for hemodynamic criterion for POTS ( $\uparrow\text{HR}\geq 30\text{bpm}$  within 10min), IOH (transient  $\downarrow\text{SBP}\geq 40\text{mmHg}$  within 15s), OH ( $\downarrow\text{SBP}\geq 20\text{mmHg}$  within 3min), and IST (supine  $\text{HR}>100\text{bpm}$ ). Categorical data were analyzed with a Fisher’s Exact test.

**RESULTS:** POTS criterion was met in 21 (30%) Long-COVID patients. IOH criterion was met in 43 (61%) patients. OH was seen in 2 patients and IST in 1 patient. Overall, 51 (73%) patients met the criterion for at least one autonomic disorder. The POTS criterion was met in 20 (36%) females, but no males ( $p=0.037$ ), whereas the IOH criterion was similarly met in females and males (63% vs. 57%;  $p=0.7$ ). The OH and IST patients were female. Overall, there was a trend for more females than males (77% vs. 51%;  $p=0.14$ ) meeting the criterion for at least one disorder.

**CONCLUSION:** Long-COVID patients have objective evidence of autonomic abnormalities, most commonly IOH, followed by POTS. IOH will be missed unless an active stand protocol is used. POTS was much more common in females than males, but IOH was equally evident between sexes. Overall, there is a trend toward increased frequency of autonomic abnormalities in females than males with Long-COVID.

#### **KEYWORDS:**

COVID-19; Autonomic; Dysfunction; Long-COVID

300 words