## Heart Failure and Cardiomyopathies

# HEART RATE VARIABILITY DURING MENTAL STRESS PREDICTS HEART FAILURE OUTCOMES IN PATIENTS WITH STABLE CORONARY ARTERY DISEASE

Poster Contributions
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**Background:** Heart failure (HF) is a common complication in patients with coronary artery disease (CAD) and leads to poor quality of life and increased mortality. Mental stress is recognized as a risk factor for HF, but the underlying mechanism is unclear. We predict that stress-induced autonomic dysfunction is associated with worse HF outcomes.

**Methods:** We examined 753 participants with stable CAD at an university-affiliated healthcare system from 2011 to 2016. Mental stress was evoked using a public speaking task and high-frequency heart rate variability (HFR HRV, signifying vagal withdrawal) was measured via Holter monitoring at rest and during mental stress. The primary outcome was a composite of acute (incident) and acute on chronic (worsening) HF in the inpatient or outpatient setting. Fine-Gray suddistribution hazard models were used.

**Results:** Participants had a mean age of 58 years, 35% were female, and 43% were Black. The median follow-up time was 5.66 years. In fully adjusted models for age, sex, race, and comorbidities, higher HFR HRV during mental stress was associated with a decreased risk of composite HF events (HR 0.80 [95% CI 0.73-0.87] per standard deviation increase, $P<.0001$). Stronger associations were observed with HF with reduced ejection fraction than HF with preserved ejection fraction, especially in fully adjusted models.

**Conclusion:** Stress-induced autonomic dysfunction predicts HF outcomes in patients with CAD and may be an independent mechanism in HF disease progression.

**Table 1: Relationship between High-Frequency Heart Rate Variability and Heart Failure Events**

| Outcomes (n) | Stress High-Frequency HRV | | | | |
|---|---|---|---|---|---|
| | Model 1 | | Model 2 | | |
| | SHR (95% CI) | P-value | SHR (95% CI) | P-value | |
| HFrEF* (n=44) | 0.76 (0.71-0.81) | P<.0001 | 0.77 (0.69-0.86) | P<.0001 | |
| HFpEF* (n=28) | 0.82 (0.71-0.95) | P=.01 | 0.91 (0.75-1.12) | P=.39 | |
| Composite (n=76) | 0.76 (0.70-0.82) | P<.0001 | 0.80 (0.73-0.87) | P<.0001 | |

| Outcomes (n) | Rest High-Frequency HRV | | | | |
|---|---|---|---|---|---|
| | Model 1 | | Model 2 | | |
| | SHR (95% CI) | P-value | SHR (95% CI) | P-value | |
| HFrEF* (n=44) | 0.87 (0.77-0.99) | P=.04 | 0.94 (0.78-1.14) | P=.54 | |
| HFpEF* (n=28) | 0.87 (0.77-0.99) | P=.04 | 0.94 (0.77-1.14) | P=.52 | |
| Composite (n=76) | 0.87 (0.78-0.97) | P=.01 | 0.94 (0.82-1.09) | P=.43 | |

*Four participants were excluded from sensitivity analyses due to unknown ejection fraction or moderately reduced ejection fraction.*

**Abbreviations: SHR**, subdistribution hazard ratio; **HRV**, heart rate variability; **HFrEF**, heart failure with reduced ejection fraction; **HFpEF**, heart failure with preserved ejection fraction.

**Model 1**: Adjusted for age, sex, and race.

**Model 2**: Adjusted for age, sex, race, active smoking, myocardial infarction, coronary artery bypass graft, percutaneous transluminal coronary angioplasty, hypertension, hyperlipidemia, diabetes mellitus, and body mass index.