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Quality of Life in Heart Failure with Preserved Ejection Fraction: Differential Associations with Exercise Performance, Daily Activity Levels and Ventricular Function

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Introduction: Patient-reported quality of life (QOL) is a highly prognostic and clinically relevant endpoint in patients with Heart Failure with preserved Ejection Fraction (HFpEF). The relationships between QOL and different markers of HF severity remain unclear. **Hypothesis:** QOL will demonstrate a stronger relationship with measures of exercise capacity compared to other disease measures. **Methods:** This is a secondary analysis of the NHLBI-sponsored RELAX, NEAT and INDIE trials to determine the relationships between QOL (assessed by the Kansas City Cardiomyopathy Questionnaire and Minnesota Living with Heart Failure Questionnaire) and different domains reflecting HF severity, including maximal aerobic capacity (peak oxygen consumption, VO₂), submaximal exercise capacity (6 minute walk distance), volume of daily activity (accelerometry), physician-estimated functional class, resting echocardiography and plasma natriuretic peptide levels. **Results:** A total of 408 unique patients with chronic HFpEF were split into tertiles of QOL scores defined as QOL-worst, QOL-intermediate, QOL-best. The QOL-worst HFpEF group was youngest, with a higher BMI and greater prevalence of diabetes but the lowest NT-proBNP levels (Table). After adjustment for age, sex and BMI; poorer QOL was associated with worse peak VO₂, 6 minute walk distance and accelerometry based measures, but no relationship was seen with NT-proBNP or indices from resting echocardiography. **Conclusions:** QOL in HFpEF is most impaired in patients who are young, obese and have diabetes, and in those with lowest NTproBNP levels, and is more robustly tied to measures of exercise capacity and reduced daily activity levels rather than elevations in NT-proBNP. These findings have major implications for the understanding of QOL in HFpEF and for the design of future clinical trials targeting symptom improvement in HFpEF.

Table. Estimated difference in surrogate measures QOL_{best} group vs QOL_{worst} group.

	Unadjusted Mean Estimate ^A (95% CI)	p-value	Adjusted* Mean Estimate (95% CI)	p-value
Log NT-proBNP	0.17 (0.03, 0.32)	0.017	0.03 (-0.11, 0.16)	0.69
Accelerometry				
Average daily accelerometry units	1603 (288, 2918)	0.017	1711 (435, 2987)	0.009
Accelerometry hours active/day (hrs)	0.92 (0.29, 1.55)	0.005	0.82 (0.20, 1.45)	0.01
Exercise performance				
6-minutes walk test (meters)	58 (29, 88)	<.001	61 (32, 89)	<.001
Peak VO ₂ (mL/kg/min)	1.03 (0.09, 1.97)	0.032	1.24 (0.35, 2.13)	0.006
Exercise Duration (min)	1.18 (0.29, 2.07)	0.010	1.57 (0.72, 2.43)	<.001
Anaerobic threshold (mL/kg/min)	0.60 (0.07, 1.13)	0.026	0.63 (0.11, 1.15)	0.02
Echocardiography				
E/e'	1.33 (-0.65, 3.30)	0.187	0.50 (-1.55, 2.56)	0.63
Left atrial volume index,	5.40 (-0.66, 11.47)	0.080	0.78 (-5.04, 6.59)	0.79

*adjusted for: age, sex, and BMI.

^AParameter estimates represent the change in predicted value for surrogate endpoint for QOL_{best} group compared to QOL_{worst} group

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Clinical Characteristics, Inpatient Management and Variables Associated with Post-Discharge Mortality in Pulmonary Arterial Hypertension; Patients Hospitalized with Right Heart Failure

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Background: Pulmonary arterial hypertension (PAH) may be associated with acute and chronic right ventricular (RV) failure and confers adverse outcomes in PAH. Given a paucity of data in understanding the management of RV failure in PAH, we sought to evaluate the characteristics of PAH patients admitted with RV failure, inpatient management strategies and the determinants of post-hospitalization mortality. **Methods:** We conducted a retrospective analysis of 41 patients with an established diagnosis of PAH, admitted for management of right heart failure or cardiogenic shock. Demographics, clinical characteristics, echocardiograms, right heart catheterization, medications use and outcome data including length of stay (LOS) and mortality were evaluated. **Results:** Our cohort had a median age of 63 years and 90% were female. Hypertension (65.6%), dyslipidemia (32%), connective tissue disease (34%), and tricuspid regurgitation (71%) were common in this cohort. 17% were admitted directly to the intensive care unit (ICU), 83% to a non-ICU setting with 9% requiring escalation of care to the ICU. Inpatient management included the use of escalating diuretic dosing (80.5%), endothelin receptor antagonists (ERA) (48.8%), phosphodiesterase inhibitors (PDE-I) (61.0%), intravenous (IV) treprostinil (36.6%), spironolactone (41.5%) and digoxin (46.3%) and inhaled nitric oxide (INO) (7.3%). Overall LOS and ICU LOS were a mean of 6 and 3.5 days respectively. Evaluation of

medications revealed a 50% increase in the proportion of patients discharged on ERAs, a 21% increase in the use of PDE-I and a 71% increase in IV treprostinil use. Inpatient mortality was 0 but post-discharge mortality was 19.5% over a median follow up period of 743 days. On Cox proportional hazard analysis, age [HR(CI): 1.1 (1.02-1.2), p=0.02], serum creatinine [HR(CI): 1.7 (1.1-2.7), p=0.02] and INO [HR(CI): 39.5 (2.5-631.5), p=0.009] were found to predict post-discharge mortality in all patients. Additionally, higher TAPSE was associated with lower mortality in patients requiring only non-ICU care [HR(CI): 0.9 (0.8-0.97), p=0.01]. **Conclusion:** RV failure treatment often involves simultaneous treatment strategies aimed at improving RV preload, afterload and contractility. Understanding patterns of contemporary management of PAH patients admitted with RV failure and the factors associated with post-hospitalization mortality is important to provide better and individualized care to these patients.

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Hemodynamic Effects of Weight Loss in Obesity: A Systematic Review and Meta-Analysis

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Objectives: We aimed to explore whether weight loss may improve central hemodynamics in obesity **Hypothesis:** Hemodynamic abnormalities in obese HFpEF patients are correlated with the amount of excess body mass, suggesting a possible causal relationship. **Methods:** We systematically searched relevant databases from inception to May 2018, without language restriction. Studies reporting invasive hemodynamic measures prior to and following therapeutic weight loss interventions in patients with obesity but no clinically-overt HF were extracted. **Results:** A total of 9 studies were identified, providing data for 111 patients. Six studies tested dietary intervention and 3 studies tested bariatric surgery. Over a median duration of 9.7 months [range 0.75 to 23], median weight loss of 43 kg [range 10-58] was associated with significant reductions in heart rate [-9 bpm, 95% CI -12 to -6, p<0.001], mean arterial pressure [-7 mmHg, 95% CI -11 to -3, p<0.001], and resting oxygen consumption [VO₂, -85 mL/min, 95% CI -111 to -60, p<0.001]. Central cardiac hemodynamics improved, manifest by reductions in pulmonary capillary wedge pressure [-3 mmHg, 95% CI -5 to -1, p<0.001] and mean pulmonary artery pressure [-5 mmHg, 95% CI -8 to -2, p=0.001]. Exercise hemodynamics were assessed in a subset of patients (n=49), where there was significant reduction in exercise pulmonary artery pressure (p=0.02). **Conclusion:** Therapeutic weight loss in obese patients without HF is associated with favorable hemodynamic effects that could improve symptoms in patients with obesity and HF. Randomized controlled trials evaluating strategies for weight loss in obesity-related HFpEF are needed.

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A Comparative Analysis of Clinical Variables Associated with Hospitalization in Pulmonary Arterial Hypertension

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Background: Pulmonary arterial hypertension (PAH) is a progressive disease, characterized by pulmonary vascular remodeling and elevation in right ventricular afterload. PAH patients are at an increased risk for right ventricular failure and premature death. Hospitalization is a common precursor to downstream morbidity and mortality in PAH. We sought to characterize clinical variables associated with hospitalization in patients with prevalent PAH. **Methods:** We conducted a retrospective analysis of 124 patients with PAH at our center from 2016 to 2019, comprising demographic data, baseline clinical characteristics, echocardiograms (TTE) and right heart catheterizations (RHC). The cohort was segregated into two groups based on whether patients were admitted to the hospital. A comparative analysis of hospitalized (n=61) vs non-hospitalized (n=63) patients was performed. Regression modeling determined predictors of admission. **Results:** 82% of patients hospitalized were related to cardiac complications of PAH whereas 18% were non cardiac hospitalizations. 67% of cardiac admissions were related to exacerbation of right heart failure or cardiogenic shock. Other causes included acute pulmonary embolism (3%), cardiac surgery (3%), chest pain (2%), supraventricular arrhythmias (5%), and AV block (2%). Hospitalized patients had significantly higher proportions of patients with age >60 years (54 vs 36%), NYHA class III symptoms (57 vs 39%), hypertension (HTN) (61 vs 40%), tricuspid regurgitation (54 vs 33%), baseline oxygen requirement (34 vs 16%), pericardial effusion (21 vs 6%) on TTE and higher mean right atrial (RA) pressure by RHC (8 vs 6 mmHg). Furthermore, admitted patients had significantly lower right ventricular fractional area change (23 vs 34%), and tricuspid annular plane systolic excursion (TAPSE) (18 vs 21mm) by TTE. On multivariate logistic regression analysis, NYHA class III [OR(CI): 12 (2-62), p=0.004], HTN [OR(CI): 4 (1.1-16.6), p=0.04] were associated with higher odds of hospitalization whereas high TAPSE was associated with lower odds of hospitalization [OR(CI): 0.87 (0.8-0.9), p=0.03]. **Conclusion:** Accurate assessment of risk factors associated with hospitalization in PAH is important as hospitalization is a sentinel event associated with downstream mortality in PAH patients. Our study provides insights into predictors of hospitalization in PAH patients and may help with regards to risk stratification in the outpatient setting.