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### P3196

#### Anorexia coexisted in frailty predicts 1-year prognosis in patients with heart failure: a multicenter prospective cohort study

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**Background:** Anorexia often coexists with heart failure (HF) and leads to malnutritional status. Particularly in fragile HF patients, anorexia may carry poor prognosis, however, detailed insight has been remained unknown.

**Purpose:** This study aimed to examine the relationship between the presence of frailty and anorexia and 1-year prognosis in HF.

**Methods:** This prospective study was performed as a multicenter cohort study in Japan (FLAGSHIP). We analyzed 1,606 ambulatory patients admitted for acute HF or exacerbation of chronic HF. From data at discharge, we collected data on frailty, anorexia, age, gender, New York Heart Association class, brain natriuretic peptide, depression (5-item Geriatric Depression Scale  $\geq 2$ ) and medications for HF treatment. Frailty was defined as  $\geq 3$  of the followings based on our previous publication: usual walking speed  $< 0.8$  m/s; grip strength  $< 26$  kg (men) or  $< 17$  kg (women); Performance Measure of Activity in Daily Living-8  $\geq 21$ ; body mass index  $< 20$  kg/m<sup>2</sup>. Anorexia was defined as Simplified Nutritional Appetite Scale  $< 14$ . Study outcome is a composite outcome of HF re-hospitalization or all-cause mortality within one year after discharge. Cox proportional hazards model was used to examine the association between measured variables and study outcome.

**Results:** A total of 257 events (16.0%) were observed (209 HF re-hospitalization, 27 cardiac death, 21 non-cardiac death). There was a significant difference in event-free survival across the groups stratified by frailty and anorexia (Log-rank test,  $p < 0.001$ ) (Figure). As the result of Cox proportional hazards model adjusted for all variables, coexistence of both frailty and anorexia was independently associated with 1-year prognosis (hazard ratio [HR] 1.73, 95% confidence interval [CI] 1.08–2.75), whereas frailty without anorexia was not (HR 1.28, 95% CI 0.84–1.96).

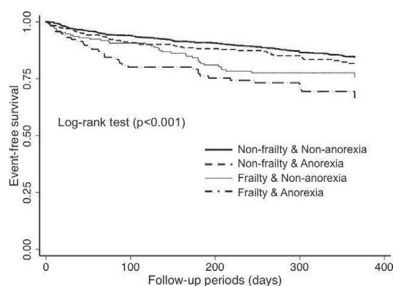


Figure 1. Kaplan-Meier curve analysis

**Conclusion:** The results of this study indicate that anorexia leads to poor prognosis in fragile HF patients and should be assessed along with frailty in clinical practice.

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#### Frailty predicts short-term heart failure re-hospitalization independently from other known prognostic indicators in patients with heart failure: a multicenter prospective cohort study

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**Background:** As prognostic impact of frailty in heart failure (HF) has been published, indistinct clinical consensus that fragile HF patients tend to be re-hospitalized earlier than the patients without frailty has been raised. To establish clinical availability, short-term prognostic value of frailty need to be examined.

**Purpose:** This study aimed to examine the predictive ability of frailty-based assessment for HF re-hospitalization within six months.

**Methods:** This prospective study was conducted as a part of a multicenter cohort study in Japan to develop frailty-based diagnostic criteria of frailty in HF patients (FLAGSHIP). We analyzed 1,606 ambulatory HF patients using data of discharge and follow-up. Study outcome was HF re-hospitalization within six months. Frailty was assessed with following three items; usual walking speed (UWS), grip strength (GS) and Performance Measure of Activity in Daily Living-8 (PMADL-8)  $\geq 21$ . A cut-off value of each indicator was identified using receiver operating characteristic (ROC) analysis to predict study outcome, and the number of frailty items was calculated for each subject. Additionally, from data set at discharge, we collected age, women, left ventricular ejection fraction  $< 40\%$ , history of HF hospitalization, brain natriuretic peptide  $\geq 200$  pg/ml, geriatric nutritional risk index (calculated using height, weight and albumin), anemia ( $< 13$  g/dl for men,  $< 12$  g/dl for women), high-sensitivity C-reactive protein, sodium, chronic kidney disease (CKD, estimated glomerular filtration rate  $< 30$  ml/min/1.73m<sup>2</sup>), depression (5-item geriatric depression scale  $\geq 2$ ), Mini-Mental State Examination and medications for HF treatment. Cox proportional hazards model was performed including all variables to identify independent predictors of short-term HF re-hospitalization.

**Results:** A total of 173 HF re-hospitalization were observed (10.8%). Cut-off value of each frailty item was as follows; UWS  $< 0.911$  m/s; GS  $< 26.8$  kg (men), 16.5 kg (women); PMADL-8  $\geq 21$ . As the results of Cox proportional hazards model, independent predictors of 6-month HF re-hospitalization were the number of frailty items (0 vs 3, hazard ratio [HR] 1.95; 95% confidence interval [CI] 1.16–3.28), history of HF hospitalization (HR 2.27; 95% CI 1.63–3.16), anemia (HR 1.48; 95% CI 0.99–2.20), CKD (HR 1.66; 95% CI 1.16–2.38), oral inotropic agent (HR 1.97; 95% CI 1.35–2.87).

**Conclusion:** Our results demonstrate that frailty becomes a novel short-term prognostic indicator for HF re-hospitalization independently from other known prognostic factors.

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## ROLE OF NON CODING RNAs IN CARDIOVASCULAR DISEASES

### P3198

#### Long noncoding RNA NEAT1 controls ROS production in macrophages and is suppressed in post-myocardial infarction patients

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**Background:** Inflammation is a key driver of atherosclerosis and myocardial infarction (MI), and beyond proteins and microRNAs, long noncoding RNAs (lncRNAs) have been implicated in inflammation control. In a previous study of circulating immune cells (PBMCs) from post-MI patients, we identified distinctive anomalies in the patients by comprehensive RNA-sequencing (RNA-seq) based transcriptome mapping (protein-coding transcripts, lncRNAs). Among deregulated lncRNAs, NEAT1 was the most highly expressed and the only one significantly suppressed in patients.

**Methods and results:** We subsequently investigated NEAT1 knockout (NEAT1<sup>-/-</sup>) mice as a model of the NEAT1 deficiency observed in post-MI patients, and thus evaluated if NEAT1 depletion may directly and causally alter immunoregulation. NEAT1<sup>-/-</sup> mice displayed a massive (6.6-fold,  $p < 0.001$ ) increase in the ROS production from NEAT1<sup>-/-</sup> macrophages ex vivo in response