Proposal for a Scientific Manuscript using the REHAB-HF Databases

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Working Title: Effects of the Multidomain Physical Rehabilitation intervention on Frailty and Relationship with Patient-Centered Outcomes in Acute Decompensated Heart Failure: Findings from the REHAB-HF trial

Goals/Objectives/Research Questions:

Among participants of the REHAB-HF trial:

Aim 1: Evaluate the interaction between baseline frailty status and treatment effects of multidomain physical rehabilitation intervention on functional status, quality of life, and risk of adverse clinical outcomes

Hypothesis: Frailty status will significantly modify the treatment effect of the multidomain physical rehabilitation intervention. The rehabilitation intervention will be associated with greater improvements in functional status, as measured by SPPB, quality of life, and lower risk of adverse clinical outcomes among frail (vs. pre-frail/non-frail) individuals.

Aim 2: Determine the association between longitudinal changes in "modified" frailty index (at 3-months) with changes in functional status as assessed by SPPB, quality of life, and risk of adverse clinical outcomes.

Hypothesis: Greater reductions in Fried frailty score will be associated with greater improvement in overall SPPB, QOL and lower risk of adverse clinical outcomes. Consistent with the primary outcomes analysis, we will use the modified Fried criteria, not factoring weight loss, for assessment of frailty status.

Study Design and Methods

Study Population:

- All participants of the REHAB HF trial

Exclusion Criteria:

- Missing follow up assessment of all outcomes of interest at 3 month follow up. If one outcome is missing, we will still use the participant for other available outcomes

Study Variables:

Primary exposure variables of interest:

- Baseline and follow-up (1-month, 3-month) measures of frailty score by Modified Fried Frailty Criteria Modified Fried Frailty Criteria excludes weight loss criteria due to difficulty in ascertaining weight changes due to fluid status.

Primary outcome of interest:

- SPPB score at 3 months follow up

Secondary outcome of interest:

- Quality-of-life (by KCCQ and Euro QOL score) at 3 months follow up
- 6-min walk distance at 3 months follow up
- Cognition score (MoCA score)
- Geriatric depression score (GDF-15)
- Clinical outcomes:

  Rates of all-cause hospitalization

  Rates of composite of all-cause hospitalization or death

Covariates:

- Baseline demographic, anthropometric, clinical characteristics as assessed among the REHAB HF participants (see Table 1)

Statistical Analysis Plan:

1. The study participants will be stratified according to baseline frailty status (frail vs. not frail), as determined by the Modified Fried Frailty Criteria, and the baseline clinical, demographic characteristics, SPPB, QOL will be compared across the two categories
2. SPPB, QOL scores, 6-minute walk distance, cognition, and depression scores at 3 months follow up will be compared between treatment arms (multidomain physical rehabilitation intervention vs. usual care) stratified by frail vs. non-frail status using analysis of covariance with adjustment for baseline measure, clinical site, EF category, age, and sex. Least square means were used to estimate intervention effects. Effect sizes were reported with 95% confidence intervals (CIs).
3. The rates of all cause hospitalization, death, and composite of all-cause hospitalization or death at 6 months follow up will be compared between treatment arms (multidomain physical rehabilitation intervention vs. usual care) stratified by frail vs. non-frail status using Poisson regression with adjustment for clinical site, EF category, age, and gender.
4. All cause hospitalization and death outcomes will also be adjusted for SPPB score
5. Effects of the intervention on proportion-based outcomes (e.g., patients with hospitalizations, patients with falls) were analyzed using logistic regression adjusted for clinical site, age, and sex
6. Adjusted models detailed in #2 to #6 will be constructed with multiplicative interaction term (frailty status X treatment arm) for each outcome of interest to determine if the treatment effects of the intervention are modified by the frailty status (by the Modified Fried Frailty Criteria) at baseline and considered significant for P-interaction < 0.1. Effect sizes in the frailty status-based subgroups will be reported regardless of the significance of the interaction test
7. Proportion of participants in the intervention and control arm will improvements in individual components of the Fried frailty score at 1-month and 3-month follow up will be compared
8. Association between change in frailty status (difference in number of frailty criteria at baseline and 3 month follow up) and outcomes at 3 months and 6 months will be assessed using adjusted regression models. Participants with interval clinical event before frailty follow up assessment will be excluded from the clinical outcomes analysis. Separate models were constructed for each outcome and for each study arm with adjustments for age, sex, clinical site, EF category, and randomization.