

Frailty Status Modifies the Efficacy of Exercise Training Among Patients with Chronic Heart Failure and Reduced Ejection Fraction: An Analysis From the HF-ACTION Trial | Pandey et al. Circulation, July 2022

STUDY HIGHLIGHTS

Objective: To evaluate whether frailty modified the treatment effect of aerobic exercise training (ET) on outcomes among patients with heart failure with reduced ejection fraction (HFrEF)

Methods: Secondary analysis of patients with stable HFrEF enrolled in HF-ACTION randomized control trial (ET vs usual care). Baseline frailty measured by Frailty Index (FI) (frail= >0.21)

Outcomes: *Primary composite end point:* all-cause hospitalization or all-cause mortality. *Secondary end points:* cardiovascular or heart failure events, quality of life (QOL), peak VO₂, & 6MWT

Analysis: Multivariable Cox proportional hazard models with interaction terms (frailty x treatment arm)

Results: Among 2130 participants, lower risk of primary composite end point in frail but not non-frail patients (mostly driven by ↓ all-cause hospitalizations); No difference in most secondary end points except for slightly greater improvement in QOL at 3 months for frail vs non-frail patients.

CENTRAL FIGURE

Table 2. Treatment Effects of Aerobic Exercise Training on Clinical Outcomes Among Nonfrail and Frail Participants

Outcomes of interest	Treatment effect of aerobic exercise training across frailty strata*				P interaction (treatment x frailty)†
	Nonfrail participants		Frail participants		
	Hazard ratio (95% CI)	P value	Hazard ratio (95% CI)	P value	
Primary composite end point	1.04 (0.87–1.25)	0.65	0.83 (0.72–0.95)	0.007	0.04
All-cause mortality	0.98 (0.66–1.47)	0.94	0.93 (0.71–1.22)	0.59	0.75
All-cause hospitalization	1.05 (0.85–1.29)	0.67	0.84 (0.72–0.99)	0.04	0.09
Heart failure hospitalization	0.80 (0.57–1.12)	0.20	0.91 (0.73–1.13)	0.39	0.56
Cardiovascular death or heart failure hospitalization	0.81 (0.57–1.15)	0.23	0.93 (0.75–1.17)	0.56	0.55
Cardiovascular death or cardiovascular hospitalization	0.90 (0.71–1.13)	0.36	0.94 (0.79–1.13)	0.51	0.77

*Stratified Cox models were constructed for frail and nonfrail participants separately and for each outcome with adjustment for the same covariates as indicated in the P interaction noted (except for the stratifying variable).
 †The interaction between treatment arm and frailty status for the risk of the primary composite end point and secondary endpoints was assessed by including a multiplicative interaction term (treatment arm x frailty status) in the most adjusted model evaluating the association of treatment with outcomes in the overall cohort with following covariates: age, sex, race, treatment arm, left ventricular ejection fraction, heart failure etiology, Beck Depression Inventory score, baseline peak exercise oxygen uptake, and atrial fibrillation. Separate models were constructed for each outcome.

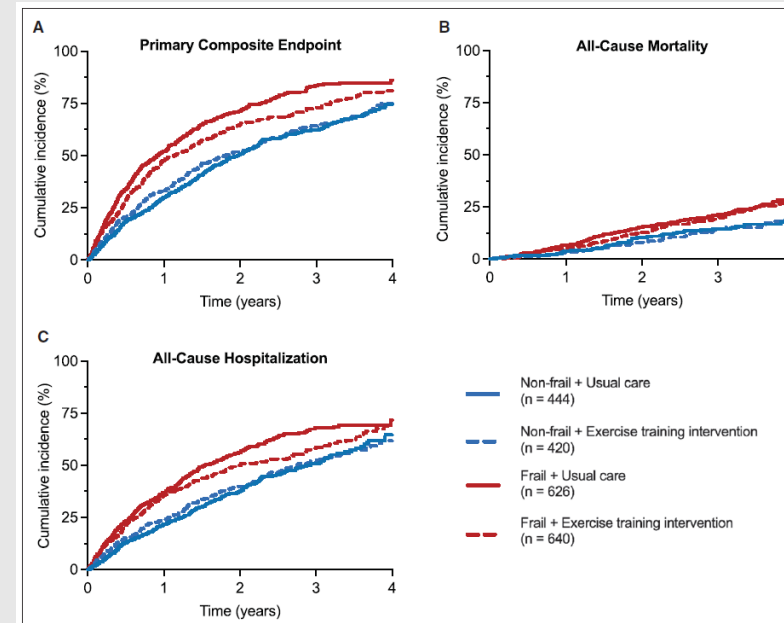


Figure 1. Cumulative incidence of the primary composite end points and its components (all-cause mortality and all-cause hospitalization) stratified by frailty status and treatment arm.
 A frailty index threshold of 0.21 was used to stratify participants into nonfrail (frailty index ≤0.21) vs frail (frailty index >0.21) groups.

REVIEWER'S COMMENTS

Frailty may identify HFrEF pts at ↑ risk for poor outcomes who are more likely to benefit from ET

- **Heterogeneity of treatment effect in RCTs:** Frailty is an important factor to consider when examining future treatment effects in RCTs.
- **Mechanisms underlying the efficacy of ET in frail patients:** ET may improve symptoms associated with frailty which in turn may ↓ all-cause hospitalization rates.
- **Translation to advanced HF:** ET may be an effective “prehab” for frail patients seeking LVAD or HTX .
- **Importance of frailty:** We need to routinely assess it, address it, and stop undertreating it.

LIMITATIONS

- Younger population & majority men (~70%) → limits translatability to older adults and women
- No objective measures of physical function
- No longitudinal assessments to determine impact of ET on changes in frailty

Oxygen Uptake During Activities of Daily Life in Patients Treated With a Left Ventricular Assist Device
 K.K Mirza et al. JHLT, March 2022

STUDY HIGHLIGHTS

Objective: To investigate the relation between oxygen consumption during activities of daily life (ADLs) and measures of functional capacity (FC) in patients with left ventricular assist device (LVAD).

Methods: Prospective study of LVAD patients and healthy controls matched on sex, body mass index (BMI), smoking status, and ethnicity.

Outcomes: Peak oxygen consumption (pVO₂) measured during cardiopulmonary exercise test (CPET). Oxygen consumption (VO₂) and % of peak VO₂ (% VO_{2peak}) measured at rest, during several ADL tasks (Figure 1), and 6-minute walk test.

Results: 15 LVAD patients and 16 healthy controls participated. All participants were older (61 ± 10 years vs 60 ± 9 years) males. Average LVAD implant time about 2 years. pVO₂ values were lower in LVAD patients (14.9 ± 2.2) compared to controls (39.6 ± 7.5). VO₂ was lower and %VO_{2peak} higher in LVAD patients vs controls (Figure 2). Durations of all ADL tasks were longer in LVAD patients.

CENTRAL FIGURE

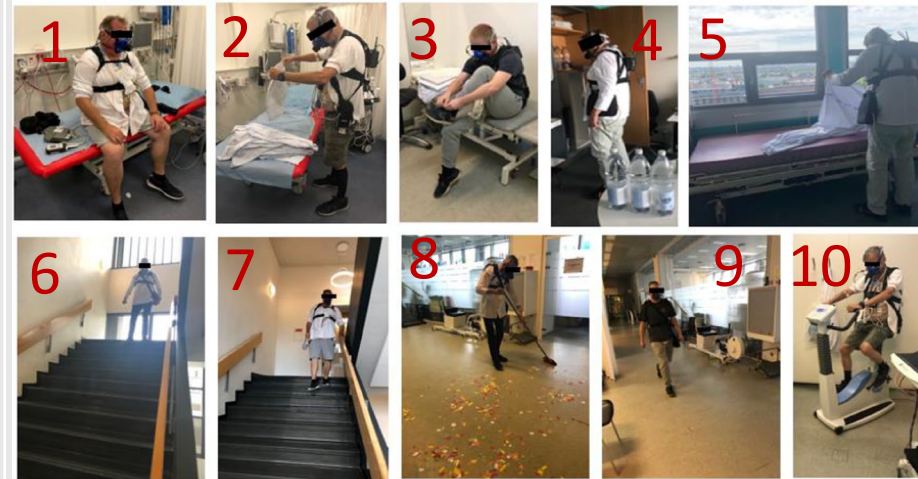
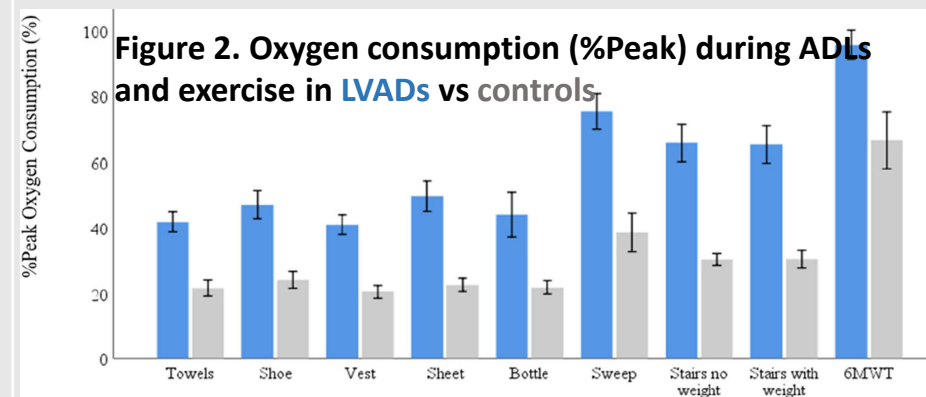


Figure 1. ADL 1: LVAD vest on; **ADL 2:** fold 10 towels; **ADL 3:** socks/shoes on; **ADL 4:** put 6 bottles in cabinet; **ADL 5:** make bed; **ADL 6:** climb stairs; **ADL 7:** climb stairs with weight; **ADL 8:** keep floor clean of confetti for 4 mins; **9:** 6 MWT; **10:** CPET



REVIEWER'S COMMENTS

%VO_{2peak} during ADLs is ↑ in LVAD vs control patients → demonstrates ↑ use of Vo₂ reserves → LVAD patients compensate by prolonging duration of tasks → may contribute to ↓ QOL

- **Novel study of patient centered outcomes in LVAD patients:** first study of oxygen consumption during ADLs and FC activities in LVAD patients
- **Role of exercise training:** exercise training may contribute to better work capacity → future studies should investigate the effect of exercise on pVO₂ and work capacity in LVAD patients.
- **Improved LVADs:** Smart pumps with the ability to ↑ flow in response to ↑ metabolic demands could ↓ effort of performing ADLs for LVAD patients.

LIMITATIONS

- Small sample size
- Single center study
- All male participants → not generalizable to females

The Relationship Between Psychological Distress and Medication Adherence in Lung Transplant Candidates and Recipients: A cross-sectional study
 Wessels-Bakker et al. *Clinical Nursing*, March 2022

STUDY HIGHLIGHTS

Objective: To determine the prevalence of psychological distress (anxiety, depression and post-traumatic stress disorder [PTSD]) and its association with medication adherence in lung transplantation

Methods: Single center cross sectional study of lung transplant candidates and recipients.

Outcomes: Symptoms of depression and anxiety assessed using the Brief Symptom Inventory; PTSD assessed using the Impact of Event Scale; medication adherence assessed using the Basal Assessment of Adherence to Immunosuppressive Medication Scale (adapted for candidates)

Results: 73 lung transplant candidates & 116 recipients included. High prevalence of depression, anxiety and PTSD in lung transplant candidates and recipients (Table 2). Symptoms of anxiety and medication adherence were significantly and positively related in recipients (p=0.048) but not in candidates. No significant relationship between depression or PTSD and adherence.

CENTRAL FIGURE

TABLE 2

Symptoms of psychological distress in lung transplant candidates and recipients

	Candidates (n = 73)			Recipients (n = 116)		
	Median (IQR)	% subclinical	% clinical	Median (IQR)	% subclinical	% Clinical
Depression	5 (3–6)	23.3	16.4	3 (3–5)	14.7	6.9
Anxiety	5 (3–6)	17.8	20.5	4 (4–6)	19.0	13.8
PTSD				4 (0–13)	21.6	12.1

Medication Adherence in past 4 weeks	Candidates N= 73	Recipients N= 116
Non-adherent	26 (36%)	48 (41%)
Missed a dose	19 (26%)	27 (23%)
Missed ≥2 doses	0	1 (1%)
Took meds >2 hours before or after prescribed time	19 (26%)	39 (34%)
Altered prescribed dose without telling professional	4 (16%)	2 (2%)
Stopped taking medications completely	0	0

REVIEWER'S COMMENTS

- **High prevalence of psychological distress** in lung transplant candidates and recipients → supports need for routine assessments in practice
- **Findings challenge previous hypothesis** that medication nonadherence mediates the relationship between depression and adverse outcomes observed in lung transplantation
- **Wide variability in time** on wait list for candidates & time since transplant surgery for recipients → psychological distress and medication adherence may be ↑ or ↓ prevalent based on timing of assessment (early/late in transplant trajectory) → need longitudinal assessments
- **Qualitative studies needed** to explore the role of anxiety in improved medication adherence.

LIMITATIONS

- Single center study → may not be generalizable to other centers
- Cross sectional design → longitudinal assessments are needed