A refined Lung Transplant Frailty Scale incorporating serum albumin is associated with risk of mortality in lung transplant candidates

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WHAT WAS KNOWN

- In lung transplantation, frailty is associated with worsened long-term health related quality of life, increased peri and post-operative complications, and increased mortality.
- We previously developed The Lung Transplant Frailty Scale (LT-FS) which has superior construct and predictive validity for poor outcomes compared to other frailty measures

RATIONALE

- Real world implementation of the LT-FS revealed day-to-day variations in C-reactive protein (CRP), a biomarker included in the LT-FS, raising concerns about its reliability
- The binary categorization (“frail” vs “not frail”) of the LT-FS lacked granularity
- Serum albumin < 3.5 mg/dL has been shown to be independently associated with higher levels of mortality after lung transplantation and greater stability than CRP
- We sought to refine the LT-FS by substituting CRP with serum albumin as a frailty biomarker
- Further, we aimed to create a three-category scoring system (“frail”, “pre-frail”, and “not-frail”) which better represents the spectrum of frailty and improve discrimination

METHODS

- This was a multicenter cohort study of lung transplant candidates ≥18 y/o at UCSF, Columbia University, and the University of Pennsylvania
- We explored substituting high serum C-reactive protein (≥10 mg/L) with low albumin (≤3.5 g/dL) as the LTFS biomarker. Other LT-FS components were not changed (Fig. 1)

Figure 1. Table comparing components of LT-FS instruments using C-reactive protein and serum albumin

	CRP	Albumin
LT-FS Base	Grip Strength	Grip Strength
	Gait Speed	Gait Speed
	High CRP	Low Albumin
LT-FS Body Composition	Grip Strength	Grip Strength
	Gait Speed	Gait Speed
	High CRP	Low Albumin
	Low ASMI	Low ASMI

Grip strength adapted from the Fried Frailty Phenotype and gait speed adapted from the Short Physical Performance Battery. ASMI quantified by bioelectrical impedance analysis using the InBody S10.

High CRP ≥10 mg/L, Low Albumin ≤3.5 g/dL, Low ASMI M≤7.3; F≤5.8

Figure 2. Kaplan-Meier plots of waitlist delisting for becoming too ill or death stratified by frail, pre-frail, and not frail groups using LT-FS Base (A) and LT-FS Body Composition (B). Kaplan-Meier plots of 3-year post-transplant survival probability stratified by frail, pre-frail, and not frail groups using LT-FS Base (C) and LT-FS Body Composition (D). Models were adjusted for age, sex, and transplant center

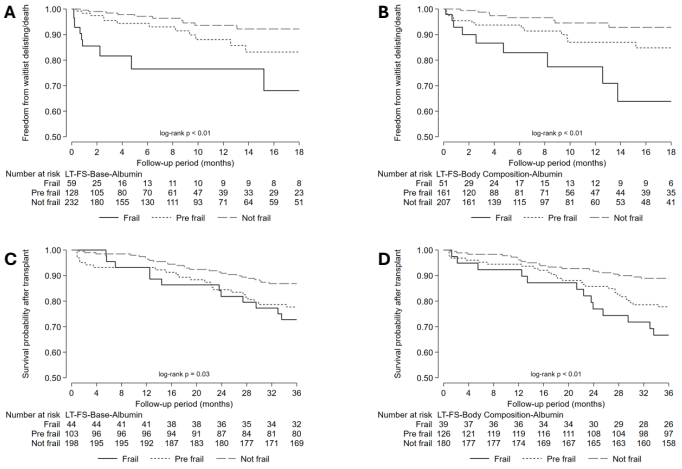

Figure 3. Relative risk of mortality between LT-FS in-groups using the adjusted Base and Body Composition models. Models were adjusted for age, sex, and transplant center. Each 1 point-worsening in LT-FS Base and LT-FS Body Composition were associated with an 11% increased risk of composite death (Base OR: 1.11, 95% CI: 1.05 to 1.16, Body Composition OR: 1.11, 95% CI: 1.06 to 1.15)

	Pre-Frail vs Not Frail			Frail vs Not Frail		
	Composite outcome	Waitlist death or delisting	3-year mortality	Composite outcome	Waitlist death or delisting	3-year mortality
LTFS-Base	1.89 (1.10, 3.23) (p = 0.021)	2.52 (1.08, 5.92) (p = 0.033)	1.66 (0.91, 3.02) (p = 0.097)	3.63 (1.94, 6.79) (p = <.001)	8.33 (3.38, 20.53) (p = <.001)	2.16 (1.08, 4.30) (p = 0.023)
LTFS-Body Composition	2.53 (1.49, 4.28) (p = <.001)	2.91 (1.22, 6.90) (p = 0.016)	2.10 (1.16, 3.78) (p = 0.014)	5.86 (2.93, 11.69) (p = <.001)	6.90 (2.61, 18.20) (p = <.001)	3.60 (1.77, 7.33) (p = <.001)

METHODS cont.

- We evaluated potential cut-points to establish LT-FS “frail”, “pre-frail”, and “not-frail” categories using Macro-Area Under the Curve, Brier Score, Max-rescaled R^2, and Spiegelhalter’s Z test
- We applied multivariable Cox models to evaluate the associations of the LT-FS as a continuous and categorical measure with a composite outcome of waitlist death or delisting or post-transplant mortality, preoperative delisting/death, and post-transplant mortality.

CONCLUSION

- Pre-frail and frail candidates had increased mortality risk by both LT-FS measures, with pre-frailty capturing an intermediate risk between non-frailty and frailty
- The refined LT-FS demonstrated strong association with death before and after transplant both as a continuous and ordinal measure

WHAT THIS STUDY ADDS

- We refine a frailty measure specific to the advanced lung disease and lung transplant community which is clinically scalable and provides an objective measure of risk
- The LT-FS identifies a graded mortality risk before and after lung transplant
- The addition of a “pre-frail” category better represents the spectrum of frailty and, if validated, may allow more nuanced assessments of potential transplant candidates

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Abbreviations: CRP, C-reactive protein; ASMI, Appendicular Skeletal Muscle Index.

Definitions of frail, pre-frail, and not frail for LT-FS Base were >19.3, ≥15.9 and ≤19.3, and <15.9, respectively; for LT-FS Body Composition, >22.2, ≥17.2 and ≤22.2, and <17.2

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