

Low Free Testosterone and Frailty Predict Overall Survival in Surgical Patients

Fangyi Lin¹, Gordon Hong², Frances Kim¹, Farha Pirani³, Salima Makhani⁴, Mark Henry, MD¹, Ian Cooke, MD¹, Reza Nabavizadeh, MD¹, Chad Ritenour, MD¹, Akanksha Mehta, MD, MS¹, Mehrdad Alemozaffar, MD¹, Viraj A. Master, MD, PhD¹, Kenneth Ogan, MD¹

¹ Department of Urology, Emory University School of Medicine, Atlanta, GA, USA; ² Northeast Ohio Medical University, Rootstown, OH, USA; ³ Medical College of Georgia, Augusta, GA, USA; ⁴ Mercer University School of Medicine, Macon, GA, USA

Introduction

- Frailty is defined as a syndrome of decreased resiliency and physiologic reserve.
- Preoperatively, frailty is predictive of higher complications and mortality.
- Male testosterone is an important contributor to factors affecting frailty. Free testosterone, specifically, plays an important role in such processes as it is the more bioactive form.

Material and Methods

- Prospectively enrolled 136 male patients undergoing major surgery requiring hospitalization from 2014-2019 at Emory University Hospital

Outcomes of Interest

- Primary outcome:** overall survival
- Secondary outcomes:** major complications (Clavien-Dindo grade \geq IIIb) and hospital readmissions

Exclusion Criteria

- Undergoing procedures impacting testosterone levels
- History of testosterone altering treatment, including chemotherapy, radiation, androgen deprivation therapy, and current medication such as testosterone supplements

Statistical Analysis

- Univariate associates: Chi-square or Fisher's exact test for categorical covariates, ANOVA for numerical covariates
- Univariate analysis between all variables with overall survival: Kaplan-Meier and log-rank methods
- Multivariate analysis to identify covariates associated with overall survival: Cox proportional hazard model
- Statistical significance was set at $p < 0.05$

Hypotheses

Low free testosterone levels will be associated with frailty and be a predictor of postoperative outcomes in patients undergoing major surgery.

Material and Methods

Data Collection

- Free and total testosterone levels were obtained during the pre-operative visit between 8:00 am and noon
- Frailty assessment: Fried Criteria¹, patients scored in ≥ 2 categories were determined as frail

Weight Loss	Unintentional weight loss of ≥ 10 lbs in the last year	
Decreased Grip Strength	BMI ≤ 24	Grip Strength ≤ 29 kg
	BMI 24.1-26	Grip Strength ≤ 30 kg
	BMI 26.1-28	Grip Strength ≤ 31 kg
	BMI > 28	Grip Strength ≤ 32 kg
Exhaustion²	≥ 2 days of exhaustion in the past week	
Low Activity	< 383 kcal/week in the past 2 weeks	
Slow Walking speed (15-ft)	Height ≤ 173 cm	Walking time $\geq 7s$
	Height > 173 cm	Walking time $\geq 6s$

4-Level Combined Frailty & T score

- Patients were divided further into 4 groups based on their frailty assessment and age-adjusted free T levels:
- Non-frail + Normal Free T
- Non-frail + Low Free T
- Frail + Normal Free T
- Frail + Low Free T

Results

Table 1: Demographics

Variable	Total Population	P-value with combined Frailty & free T score
Age at time of surgery, mean \pm SD	62.08 \pm 10.17	0.0007
Race, n (%)		0.7473
White	90 (66.18)	
BMI (kg/m²), mean \pm SD	29.81 \pm 6.26	0.1417
Surgery Technique, n (%)		0.3433
Open	54 (39.71)	
Robotic	43 (31.62)	
Laparoscopic	28 (20.59)	
Other	7 (5.15)	
Surgery Division, n (%)		0.0906
Urology	119 (87.50)	
Other	17 (12.50)	

Results

Table 2: Surgical Outcomes

Variable	Total Population (n=136)	P-value with Frailty only	P-value with Combined Frailty & free T score
Major Complications (Grade $\geq 3b$), n (%)	11 (8.09)	0.1248	0.0832
Readmission, n (%)			
30-day Readmission	15 (11.03)	0.5195	0.8113
90-day Readmission (out of 129 pts)	18 (13.95)	0.7617	0.5831
Mortality, n (%)			
30-day Mortality	3 (2.21)	0.1300	0.1870
90-day Mortality (out of 134 pts)	3 (2.24)	0.1257	0.1839
1-year Mortality (out of 107 pts)	7 (6.54)	0.0265	0.0358
Death Ever	15 (11.03)	0.0436	0.0449

Table 3: Association between low free T and Frailty

	Free T levels, n (%)		P-value
Categories of Frailty, n (%)	Normal Free T	Low Free T	
Non-frail (score 0-1)	71 (52.21)	34 (25.00)	0.0004
Frail (score 2-5)	10 (7.35)	21 (15.44)	

Results

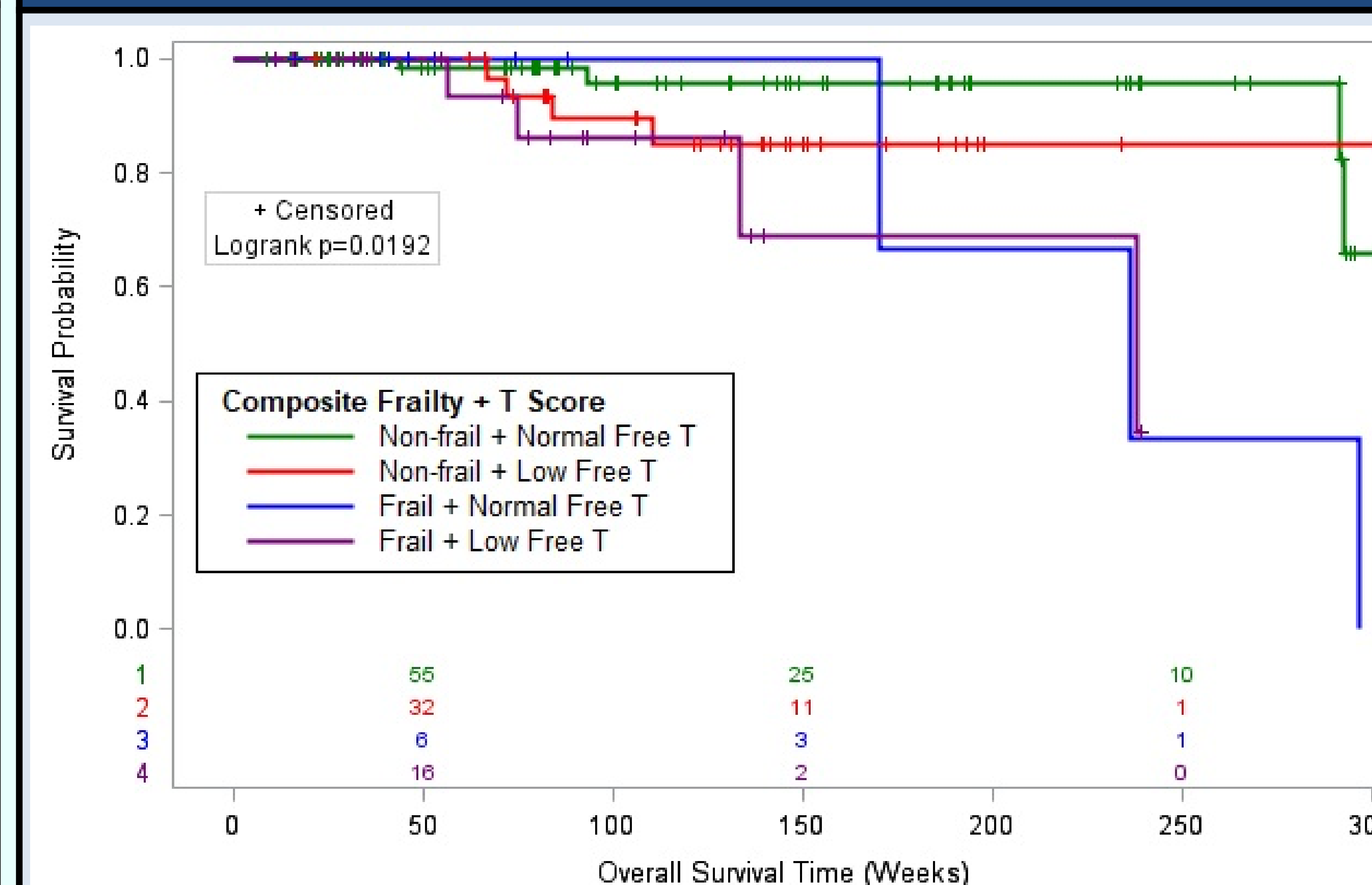


Figure 1. Kaplan-Meier Curve displays the overall survival of patients following major procedures in all four levels of the composite system with frailty score and free testosterone level combined (n=136). The log-rank test indicates a significant difference between the survival curves. Frail patients with low free testosterone levels have over a six-fold increased risk of mortality when compared to non-frail patients with normal testosterone.

Conclusions

- Low free T is associated with Frailty.
- Frailty and free T combined are predictive of 1-year mortality and overall survival.
- The addition of free testosterone with a frailty assessment has greater potential to identify surgical patients at higher risks than frailty measures alone.

References

- Fried LP et al., J. Gerontol. A Biol. Sci. Med. Sci., 2001.
- Radloff LS, Appl. Psychol. Meas., 1977.