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Sex-Specific Associations of Nutritional and Metabolic Reserves With Frailty in Chronic Kidney Disease

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Objectives : Frailty in chronic kidney disease (CKD) is associated with risk of disability and accelerated renal function decline. However, sex differences in frailty risk and the extent to which nutritional and metabolic characteristics contribute to frailty in men and women with CKD remain unclear. This study aimed to evaluate the associations of nutritional and metabolic characteristics with frailty in CKD patients, overall and stratified by sex.

Methods : This study included 5,212 patients with CKD from the Taipei Medical University Clinical Research Database between 2008 and 2019. Frailty was quantified using a cumulative deficit-based multimorbidity frailty index (mFI). Deficits were identified using the first three digits of ICD-9 diagnostic codes and were considered present if patients had ≥ 3 outpatient primary/secondary diagnoses at least 28 days apart or ≥ 1 inpatient primary diagnosis. Diagnoses with a prevalence $> 2\%$ were retained as deficit items. The mFI was calculated as the number of deficits present divided by the total number of deficit items. Multivariable logistic regression assessed associations between nutritional/metabolic characteristics and frailty, overall and by sex.

Results : The mean age of participants was 62.9 ± 13.3 years, and 44.3% were female. In the overall multivariable model, male was associated with lower odds of frailty (OR 0.800, 95% CI 0.699–0.914), whereas older age was associated with higher odds. Higher serum albumin (OR 0.774, 95% CI 0.693–0.865), total cholesterol (OR 0.995, 95% CI 0.994–0.997), and HbA1c (OR 0.941, 95% CI 0.899–0.986) were inversely associated with frailty. In sex-stratified analyses, albumin and total cholesterol remained inversely associated with frailty in both females and males. HbA1c was inversely associated with frailty in females but not in males.

Conclusions : Higher serum albumin and total cholesterol levels were associated with lower odds of frailty among patients with CKD. These findings underscore the importance of nutritional and metabolic profiles while revealing sex-specific associations in frailty.



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Table 1. Baseline Characteristics of Patients with Chronic Kidney Disease, Stratified by Gender and Frailty Status (n=5212)

Variable	Overall, n (%)	Female (n=2310)	Male (n=2902)	p-value	Female		p-value	Male		p-value
					Non-frail	Frail		Non-frail	Frail	
Marital Status										
Single / Unmarried	1185(42.7)	531(41.71)	654(43.54)	0.3512	279(46.5)	252(37.4)	0.0011	381(47.8)	273(38.7)	0.0004
Married / Partnered	1590(57.3)	742(58.29)	848(56.46)		321(53.5)	421(62.6)		416(52.2)	432(61.3)	
Age	62.90(13.26)	64.95(12.71)	61.26(13.47)	<.0001	64.13(13.52)	65.78(11.78)	0.0017	59.70(13.63)	63.24(12.99)	<.0001
Physical examination										
BUN, mg/dL	43.40(35.42)	43.25(35.48)	43.52(35.37)	0.7811	42.61(35.19)	43.87(35.76)	0.3986	42.55(34.79)	44.73(36.06)	0.1023
Uric Acid, mg/dL	6.64(2.03)	6.54(2.03)	6.72(2.03)	0.0021	6.52(2.01)	6.55(2.05)	0.6832	6.75(1.91)	6.68(2.15)	0.3796
Total Cholesterol, mg/dL	177.02(46.72)	184.96(48.84)	170.79(44.01)	<.0001	193.07(49.62)	178.28(47.18)	<.0001	174.71(43.21)	166.62(44.49)	<.0001
Triglycerides, mg/dL	149.29(95.08)	159.14(101.13)	141.54(89.30)	<.0001	158.86(102.78)	159.38(99.71)	0.9059	147.72(90.06)	134.55(87.95)	0.0002
HDL, mg/dL	42.91(13.82)	46.17(14.55)	40.39(12.65)	<.0001	46.68(15.45)	45.79(13.85)	0.2235	40.18(12.54)	40.58(12.77)	0.4799
LDL, mg/dL	94.45(33.17)	96.55(33.87)	92.82(32.53)	0.0002	100.38(34.44)	93.16(33.01)	<.0001	94.62(32.19)	90.75(32.80)	0.0026
Albumin, g/dL	4.03(0.63)	4.00(0.60)	4.06(0.65)	0.0032	4.04(0.61)	3.96(0.59)	0.0058	4.11(0.66)	4.00(0.63)	<.0001
Creatinine, mg/dL	3.76(3.52)	3.41(3.01)	4.04(3.87)	<.0001	3.38(3.11)	3.44(2.89)	0.655	3.95(3.83)	4.15(3.91)	0.2496
HbA1c, %	6.79(1.48)	6.75(1.47)	6.81(1.48)	0.2104	6.87(1.50)	6.65(1.44)	0.0004	6.90(1.50)	6.70(1.46)	0.0007
Multimorbidity frailty index	0.28(0.14)	0.29(0.14)	0.27(0.14)	<.0001	0.18(0.07)	0.40(0.09)	<.0001	0.17(0.07)	0.40(0.09)	<.0001
Frailty Severity ^a										
Fit	1465(28.11)	580(25.11)	885(30.50)	<.0001						
Mild frailty	1329(25.50)	588(25.45)	741(25.53)							
Moderate frailty	1260(24.17)	580(25.11)	680(23.43)							
Severe frailty	1158(22.22)	562(24.33)	596(20.54)							
Frailty Status ^b										
Non-frail	2794(53.61)	1168(50.56)	1626(56.03)	<.0001						
Frail	2418(46.39)	1142(49.44)	1276(43.97)							

^a The Multimorbidity Frailty Index (mFI) was categorized into quartiles: fit, mild, moderate, and severe frailty.

^b Frailty status was dichotomized into Non-frail (fit/mild) and Frail (moderate/severe) based on the mFI distribution

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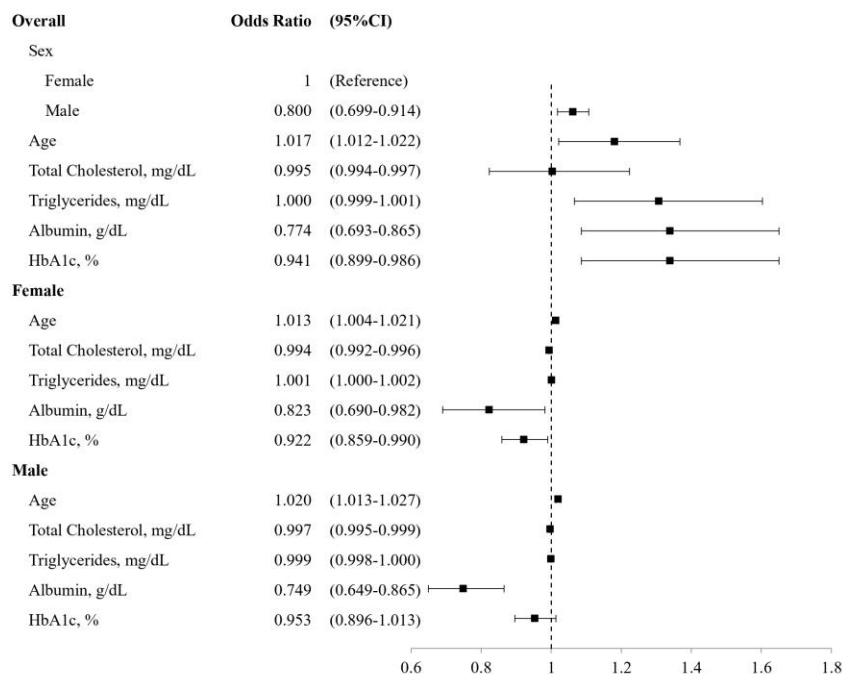


Figure 1. Factors Associated with Frailty in CKD Patients Stratified by Gender

Note: Multivariable logistic regression was used to identify independent predictors of frailty in the entire cohort and within gender-stratified subgroups.