Title

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Permalink

https://escholarship.org/uc/item/0239x3dt

Journal

Nephrology Dialysis Transplantation, 36(12)

ISSN

0931-0509

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Publication Date

2021-12-02

DOI

10.1093/ndt/gfaa323

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Frailty and the risk of kidney function decline in the elderly population: the Rugao Longevity and Ageing Study

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ABSTRACT

Background. The diverse risk factors for kidney impairments suggest that kidney function decline is more likely to occur in individuals with a broadly constituted health deficit. Here we conducted a longitudinal cohort study to evaluate the association of baseline frailty status with the risk of estimated glomerular filtration rate (eGFR) decline.
Methods. Overall, 1269 participants aged 70–84 years from Rugao Longevity and Ageing cohort with 3-year follow-up were included. Frailty was measured using a modified Fried frailty assessment. GFR was estimated using the Chronic Kidney Disease Epidemiology Collaboration equation. Associations between baseline frailty status and rapid eGFR decline were examined by multinomial logistic analysis. A linear mixed-effect model was used to determine eGFR decline in mL/min/1.73 m^2 over the study period comparing those with frail or prefrail at baseline versus those with robust status.
Results. The mean ($\pm$ standard deviation) age of participants was 75.1 ± 3.8 years. A total of 144 (11%) participants had rapid eGFR decline by at least 10% during the 3-year follow-up. Compared with robust status, baseline frail status was associated with a 2.48-fold [95% confidence interval (CI) 1.24–4.95] increased risk of rapid eGFR decline after multiple adjustments. In multivariate linear mixed model analysis, subjects with frail status but not prefrail status at baseline had a significant coefficient of -1.70 (95% CI -3.35 to -0.04) for the frail $\times$ visit term, which indicates an accelerated eGFR decline compared with robust subjects over the study period ($P = 0.044$).
Conclusions. Frailty may serve as an independent biomarker to predict the decline of kidney function.

Keywords: frailty, kidney function decline, longitudinal cohort, risk factor

INTRODUCTION

Low glomerular filtration rate (GFR), independently associated with mortality regardless of age [1, 2], is the 12th leading risk factor for death at the global level, and the 14th risk factor for disability-adjusted life-years among 79 risk factors [3]. GFR decline with age in elderly is common and the degree of progression increases particularly for persons with a lower GFR [4]. Thus, identifying higher risk elderly for early prevention is important to prevent or delay progressing to kidney failure or other adverse outcomes. Traditional factors predisposing to the deterioration of kidney function include older age, male, diabetes mellitus (DM) , hypertension (HBP), metabolic syndrome, etc. [5]. Novel risk factors for chronic kidney disease (CKD) are continuously being proposed, such as obstructive sleep apnea, higher heart rate, higher uric acid, etc. [6].

The diversity of risk factors for kidney function decline may itself be informative, which suggests that kidney function decline is more likely to occur in people with a broadly constituted general health deficits that may not necessarily cross disease thresholds. Elderly individuals in this venerable state are generally referred to as frail [7–9], which is now a recognized public health problem with a prevalence of 4–17% in persons ≥ 65 years [10]. Frailty is a state of age-related deficit accumulation that begins at the cellular level and leads to a loss of redundancy in organ systems [11]. Cellular senescence, low-grade

KEY LEARNING POINTS

What is already known about this subject?

- it has been reported that low baseline estimated glomerular filtration rate (eGFR) was associated with the incidence of frailty;
- the pathologic change of frailty indicates it may also be a predictive factor of kidney function decline;
- however, the association between frailty and future decline of kidney function in community-dwelling individuals has not been explored.

What this study adds?

- compared with robust status, baseline frail status was associated with a 2.48-fold [95% confidence interval (CI) 1.24–4.95] increased risk of rapid eGFR decline after multiple adjustments; and
- subjects with frail status but not prefrail status at baseline had a significant coefficient of −1.70 (95% CI −3.35 to −0.04) for the frail × visit term, which indicates an accelerated eGFR decline compared with robust subjects over the study period ($P = 0.044$) by multivariate linear mixed model analysis.

What impact this may have on practice or policy?

- frailty may serve as an independent biomarker to predict the decline of kidney function; and
- prevention of kidney impairment in community-dwelling elderly may be benefit from improving frailty.

inflammation, loss of telomeric structures, increased free radical production, mitochondrial dysfunction and poor DNA repair capability gradually occur in the biologic process of overall ageing [12], including renal ageing [13, 14]; however, they accelerate in the pathological process of frailty [7]. Therefore, frailty may additionally accelerate renal injury and provide an integrative perspective in the prevention of renal disease. People recognized as frail have a higher probability of developing adverse clinical events such as disability, hospitalization, falls and death. Besides, frailty was also recognized as predictor of organ or disease-based outcomes including coronary disease, heart failure and dementia in the elderly population [15–17]. These all contribute to the decline of kidney function. However, the association between frailty and future decline of kidney function in community-dwelling individuals has not been explored.

Therefore, we hypothesized that frailty in elderly people may confer a risk of kidney impairments. To test this hypothesis, we categorized an old cohort population into robust, prefrail and frail groups according to their baseline frailty status, and investigated their associations with longitudinal kidney function decline, which was defined by creatinine-based estimated GFR (eGFR).

MATERIALS AND METHODS

Study population

We used data from the ageing arm of the Rugao Longevity and Ageing Study, a community-based longitudinal study conducted in Rugao city, Jiangsu, China. As previously described [18, 19], 1788 elders aged 70–84 years were recruited at baseline

(November to December 2014, Wave 1) from 31 rural communities of Jiang'an Township, Rugao. A follow-up survey was conducted 1.5 years later (April to June 2016, Wave 2) and 3 years later (November to December 2017, Wave 3) for repeated measurement of baseline variables and for collection data on mortality and disease events onset. Of the 1788 participants who entered the cohort at Year 2014, 119 died before Wave 3, 369 withdrew from this cohort, the number of participants in Wave 3 reached 1950 with 650 newly entered individuals. We then excluded 992 individuals who had only one visit either at baseline or at Wave 3, and 104 individuals who had missing data on creatinine or frailty of baseline. Our final study population consisted of 1269 individuals (Figure 1). The Human Ethics Committee of the School of Life Sciences, Fudan University, Shanghai, People's Republic of China, approved this study. Written informed consent was obtained from all participants prior to the study.

Demographic, clinical and laboratory measures

A structured questionnaire was administered by trained field staff that delved into areas including demographic characteristics, comorbidities and medications. Fast blood samples were drawn using uniform techniques for laboratory examination at recruitment and follow-up visit of study. All laboratory values that were routinely examined in clinical diagnosis were considered and measured using Beckman AU5821 (US) clinical chemistry analyzer with standard laboratory techniques.

Estimation of GFR and change in GFR

Serum creatinine concentration was measured according to an enzymatic method with the Cica Creatinine reagent
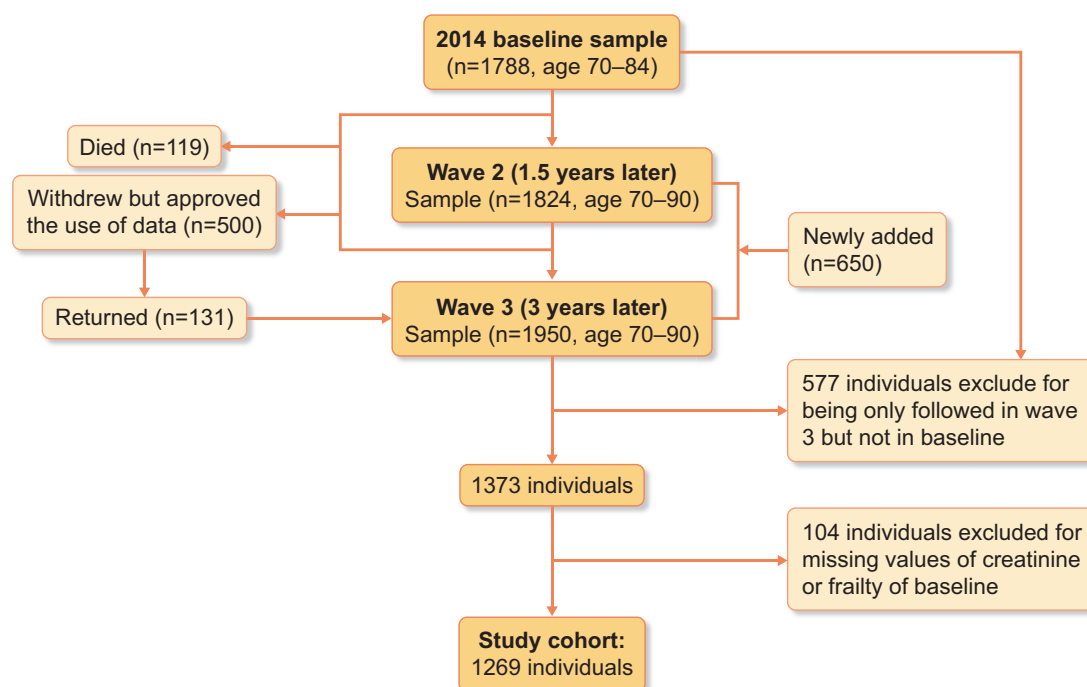
FIGURE 1: Cohort construction.

(KANTO Chemical, Tokyo, Japan). We calculated eGFR using the creatinine-based CKD Epidemiology Collaboration equation (CKD-EPI) [20].

We defined change of kidney function as percentage change in eGFR from baseline to the 3-year follow-up. The 11% of the cohort with the largest decline in $eGFR_{EPI}$ corresponded to the least loss of 10% throughout 3 years (i.e. at a rate of annual loss of 3 mL/min/1.73 m^2 for participants with GFR of 90 mL/min/1.73 m^2); We used this as a cut-off value for 'rapid decline', representing a magnitude of change that is three times the rate previously described in studies of normal aging, and that was beyond the range of noise in measurement [21]. The 65% of the cohort with the smallest decline in $eGFR_{EPI}$ corresponded to the most loss of 3.3% throughout 3 years (i.e. approximately to a largest annual loss of 1 mL/min/1.73 m^2 for participants with eGFR of 90 mL/min/1.73 m^2); we used this as a cut-off value for 'no decline', representing a change of normal aging. The rest of the participants were categorized as with mild-to-moderate decline of eGFR.

Frailty

According to Fried *et al.*, five components including unintentional weight loss, weakness, exhaustion, slowness and low activity were used to define the frailty phenotype [22, 23]. A modified Fried frailty assessment was used in this study. In brief, unintentional weight loss, exhaustion and low activity were based on self-reported items including 'weight has

decreased by 4.5 kg or 5% during the last 12 months', 'feeling tired all of the time (at least 3 or 4 days per a week)' and 'needing help to walk'. Slowness was defined as being below the 20th sex-specific percentile in gait speed, which was assessed using a Timed Up and Go test [24]. Weakness was defined as 'unable' or 'some difficulties' in lifting or carrying something as heavy as 10 kg or in squatting, which was similar to that used in other studies [23]. Participants with three or more of the five components were defined as 'frail', one or two as 'prefrail' and none as 'robust'.

Statistical analyses

Population characteristics were presented stratified by baseline frailty categories. Differences in baseline characteristics between included versus excluded participants were compared by standardized differences due to the large sample size of this study. We used non-parametric trend tests to assess differences in baseline characteristics across frailty categories. Baseline frailty status was treated as categorical variables, and its associations with change of eGFR were examined by multinomial logistic analysis. For each analysis, we employed hierarchical adjustment with three models as follows:

(i) Model 1, which included baseline frailty status;
(ii) Model 2, which included the above variables plus age, sex and education (illiterate, literate), smoking (non-

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Table 1. Baseline characteristics of 1269 participants stratified by frailty categories (robust, prefrail and frail)

Characteristics	Total, $n = 1269$	Robust, $n = 707$	Prefrail, $n = 484$	Frail, $n = 78$	P-value
Age, years	75.1 ± 3.8	74.5 ± 3.6	75.6 ± 3.9	76.7 ± 4.0	<0.001
Male, %	579 (45.6)	356 (50.4)	210 (43.4)	13 (16.7)	<0.001
Married, %	1253 (99.3)	699 (99.4)	477 (99.0)	77 (100)	0.80
Education: illiterate, %	678 (53.9)	342 (48.8)	280 (58.5)	56 (72.7)	<0.001
Occupation: peasant, %	1131 (89.3)	604 (85.7)	451 (93.3)	76 (97.4)	<0.001
Comorbidities, %					
DM	87 (6.9)	42 (5.9)	33 (6.8)	12 (15.4)	0.02
HBP	568 (44.8)	309 (43.7)	221 (45.7)	38 (48.7)	0.33
CVD	241 (19.0)	100 (14.1)	110 (22.7)	31 (39.7)	<0.001
COPD	56 (4.4)	17 (2.4)	32 (6.6)	7 (9.0)	<0.001
Stroke	104 (8.2)	42 (5.9)	46 (9.5)	16 (20.5)	<0.001
Drinking, %	248 (19.6)	175 (24.8)	67 (13.9)	6 (7.8)	<0.001
Smoking, %	321 (25.4)	195 (27.7)	114 (23.6)	12 (15.6)	0.01
Body mass index, kg/m^2	24.2 ± 3.5	24.1 ± 3.3	24.1 ± 3.6	24.7 ± 4.2	0.71
Systolic blood pressure, mmHg	156.1 ± 21.8	156.6 ± 21.9	155.9 ± 21.8	153.8 ± 21.5	0.54
Diastolic blood pressure, mmHg	82.0 ± 11.5	82.1 ± 11.1	82.1 ± 12.4	81.3 ± 9.8	0.80
eGFR, mL/min/1.73 m^2 (by CKD-EPI equation)	88.0 ± 10.1	88.7 ± 9.0	87.3 ± 11.0	85.7 ± 12.7	0.01
Laboratory variables					
Albumin, g/L	46.35 ± 2.57	46.32 ± 2.58	46.34 ± 2.53	46.77 ± 2.64	0.22
Creatinine, mg/dL	0.69 ± 0.17	0.70 ± 0.16	0.69 ± 0.17	0.66 ± 0.19	0.04
Uric acid, mg/dL	5.52 ± 1.44	5.50 ± 1.33	5.57 ± 1.57	5.45 ± 1.60	0.68
Triglyceride, mg/dL	123.89 ± 86.73	122.12 ± 84.96	125.66 ± 89.38	136.28 ± 80.53	0.02
Cholesterol, mg/dL	197.68 ± 34.36	198.46 ± 34.36	197.30 ± 35.52	194.59 ± 28.96	0.36
LDL cholesterol, mg/dL	107.72 ± 25.87	108.49 ± 25.87	107.34 ± 25.48	104.63 ± 24.32	0.31
HDL cholesterol, mg/dL	56.76 ± 12.74	57.14 ± 12.36	55.98 ± 13.13	55.60 ± 13.51	0.07
C-reactive protein, mg/L	1.8 (1.3–3.1)	1.8 (1.2–2.9)	1.9 (1.3–3.3)	2.0 (1.2–3.1)	0.05

Values are expressed as mean ± standard deviation, median (interquartile range) or percentage, as appropriate.
Conversion factors for units: albumin in g/dL to g/L, ×10; creatinine in mg/dL to μmol/L, ×88.4; uric acid in mg/dL to μmol/L, ×59.48; triglyceride in mg/dL to mmol/L, ×0.0113; cholesterol in mg/dL to mmol/L, ×0.0259; LDL cholesterol in mg/dL to mmol/L, ×0.0259; HDL cholesterol in mg/dL to mmol/L, ×0.0259.

smoker, smoker), baseline eGFR categories (<86, 86–92 and ≥ 92 mL/min/1.73 m^2), HBP and DM; and

(iii) Model 3, which included the above variables plus serum low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglyceride, albumin, uric acid and log-transformed urine albumin-to-creatinine ratio (ACR) at the 3-year follow-up due to its skewed distribution.

A linear mixed-effect model was used to compare changes from baseline to the 3-year follow-up (Wave 3) of eGFR in mL/min/1.73 m^2 between subjects with frail status at baseline and those with robust status, or between subjects with prefrail status and those were robust. In the multivariate mixed model, eGFR value at both points was a response variable, terms of baseline frailty status, visit, baseline frailty status × visit interaction, baseline age × visit interaction, sex, education, smoking, HBP and DM were treated as fixed categorical effects, LDL, HDL, triglyceride, albumin, uric acid at each visit and age at baseline, urine ACR at the 3-year follow-up were continuous covariates. Since more rapid progression is observed in those with lower eGFR, we classified eGFR into three categories based on the tertile of baseline eGFR (<86, 86–92 and ≥ 92 mL/min/1.73 m^2) and included baseline eGFR categories × visit interaction as a fixed categorical effect. We included a random intercept and random slope for each subject in the model. Results are presented as the regression coefficient [95% confidence interval (CI)] for the relation between eGFR and visit, eGFR and baseline frailty status, eGFR and baseline frailty status × visit interaction.

The frequency of missing data was 15.7% for urine ACR, <1% for smoking and education. Multiple imputation methods with five data sets were used in all regression analyses. Analyses were conducted using STATA MP version 13.1 (StataCorp, College Station, TX, USA). Significance was set at $P < 0.05$.

RESULTS

Demographic and clinical characteristics of study participants at baseline

Figure 1 depicts the selection process of the cohort participants. Wave 2 data were not included in this analysis due to short follow-up period with regard to GFR changes. Overall, 1269 individuals aged 75 ± 4 years were included and followed up for 3 years in the present analysis. The demographic and clinical characteristics of study participants at baseline according to frailty status (robust, prefrail and frail group) were described in Table 1. From robust group to prefrail group, and then to frail group, participants were older, more females, less educated, more likely to be peasant, more often had DM, cardiovascular diseases (CVDs), chronic obstructive pulmonary disease (COPD) and stroke, less alcohol drinkers and cigarette smokers, had lower eGFR levels and creatinine levels, and higher serum triglyceride levels.

Compared with 1096 excluded participants who only had one-time evaluation at baseline or Wave 3 or who lacked data on either baseline creatinine or frailty, 1296 included participants were more likely to be younger, had lower prevalence of

Table 2. Associations of baseline frailty status with change of eGFR

Frailty status at baseline	Participants number		Change of GFR: rapid decline versus no decline					
	Rapid decline	No decline	Model 1		Model 2		Model 3	
			OR (95% CI)	P-value	OR (95% CI)	P-value	OR (95% CI)	P-value
Robust	68	472	Ref		Ref		Ref	
Prefrail	59	307	1.33 (0.91, 1.95)	0.134	1.24 (0.83, 1.86)	0.300	1.28 (0.85, 1.93)	0.244
Frail	17	44	2.68 (1.45, 4.96)	0.002	2.28 (1.15, 4.51)	0.018	2.48 (1.24, 4.95)	0.010
			Change of GFR: moderate decline versus no decline					
	Moderate decline	No decline	Model 1		Model 2		Model 3	
			OR (95% CI)	P-value	OR (95% CI)	P-value	OR (95% CI)	P-value
Robust	167	472	Ref		Ref		Ref	
Prefrail	118	307	1.09 (0.82, 1.43)	0.557	1.07 (0.81, 1.42)	0.634	1.05 (0.79, 1.40)	0.726
Frail	17	44	1.09 (0.61, 1.96)	0.769	1.02 (0.55, 1.88)	0.954	1.03 (0.56, 1.90)	0.932

Model 1 includes baseline frailty status. Model 2 includes baseline frailty status plus age, sex, education (illiterate, literate), smoking (non-smoker, smoker), baseline eGFR categories, HBP and DM. Model 3 includes the variables in Model 2 plus LDL, HDL, triglyceride, albumin, uric acid and log-transformed urine ACR.

Table 3. The changes (95% CIs) of slope coefficients of eGFR by predictive variables in univariate and multivariable linear mixed model analyses

Compared with robust	Regression coefficient (95% CI)	P-value
	Univariate analysis	
Prefrail	−1.39 (−2.55 to −0.22)	0.020
Frail	−2.97 (−5.33 to −0.61)	0.013
Visit	−1.75 (−2.30 to −1.21)	<0.001
Prefrail × visit	−0.38 (−1.23 to 0.48)	0.389
Frail × visit	−2.14 (−3.87 to −0.41)	0.015
	Multivariate analysis[a]	
Prefrail	0.01 (−0.67 to 0.69)	0.978
Frail	−0.24 (−1.63 to 1.14)	0.731
Visit	−2.00 (−3.46 to −0.55)	0.007
Prefrail × visit	−0.24 (−1.06 to 0.57)	0.558
Frail × visit	−1.70 (−3.35 to −0.04)	0.044

[a]In this multivariable linear mixed model, eGFR value at both visits (baseline and the third year follow-up) was a response variable, terms of baseline frailty status, visit, baseline frailty status × visit interaction, baseline eGFR categories × visit interaction, baseline age × visit interaction, sex, education, smoking, HBP and DM were treated as fixed categorical effects, and LDL, HDL, triglyceride, albumin, uric acid at each visit and age at baseline, urine ACR at the third year follow-up were continuous covariates.

COPD, higher GFR and uric acid, and lower HDL (standardized difference >0.2; Supplementary data, Table S1).

Associations of baseline frailty status with rapid eGFR decline

A total of 144 (11%) participants had rapid decline of GFR by at least 10% during 3 years. Compared with the robust group, baseline frail group was associated with an increased risk of 3-year rapid decline in renal function [odds ratio (OR) = 2.68, 95% CI 1.45–4.96]. The association remained significant after multiple adjustments of previously reported confounders, with an OR of 2.48 (95% CI 1.24–4.95) (Table 2; Models 1, 2 and 3). No associations were observed between baseline frail status and moderate decline in kidney function, or between prefrail status at baseline and rapid decline in kidney function (Table 2; Models 1, 2 and 3). Besides, the results were very similar if we added age squared in the multivariate logistic model for the

concern that the association of age with eGFR decline may not be linear (Supplementary data, Table S2).

Baseline frailty status and changes of eGFR over the study period

The magnitude of change in eGFR in subjects with baseline frail status or prefrail status versus subjects with baseline robust status is seen in Table 3. In univariate linear mixed model analysis, eGFR declined by 1.75 (95% CI 2.3–1.21, $P < 0.001$) mL/min/1.73 m² at the second visit (Wave 3, Year 2017). Besides, subjects with baseline prefrail status had further eGFR decline of 1.39 (95% CI 2.55–0.22, $P_{for\ prefrail} = 0.020$) and 0.38 (95% CI 1.23 to −0.48, $P_{for\ prefrail\ \times\ visit} = 0.389$) mL/min/1.73 m² compared with subjects with baseline robust status. Subjects with baseline frail status had further eGFR decline of 2.97 (95% CI 5.33–0.61, $P_{for\ frail} = 0.013$) and 2.14 (95% CI 3.87–0.41, $P_{for\ frail\ \times\ visit} = 0.015$) mL/min/1.73 m² compared with subjects with baseline robust status. In multivariate linear mixed model analysis, eGFR declined by 2.00 (95% CI 3.46–0.55, $P = 0.007$) mL/min/1.73 m² at the second visit. Subjects with baseline prefrail status had no significant further decline of eGFR compared with subjects with baseline robust status. However, subjects with baseline frail status had a faster eGFR decline of 1.70 (95% CI 3.35–0.04, $P_{for\ frail\ \times\ visit} = 0.044$) mL/min/1.73 m² compared with subjects with baseline robust status.

DISCUSSION

In this study, for the first time, we provided evidence that baseline frailty was independently associated with increased risk of decline of kidney function. Our study suggests that other than modifying traditional kidney risk factors, prevention of kidney impairment in high-risk elderly individuals may be benefit from improving frailty.

The prevalence rate of frailty and prefrailty in our study was 6% and 38%, respectively, which suggests a high burden of vulnerable elderly people in China. Frailty measure is crucial for

the development of interventions against age-related conditions in older persons, and two major measurements are frailty phenotype and frailty index. Different from frailty index, which is composed by a long checklist of clinical conditions and diseases, frailty phenotype is based on a pre-defined set of five criteria, and is well served for differentiating those having early clinical symptoms of disability [25]. This frailty state is independently linked to clinical diseases such as CVDs, dementia, fracture, and disease-related mortality and hospitalization [15, 16, 26, 27]. Therefore, it has received an increasing amount of attention.

In this study, we found that frailty status was associated with levels of eGFR in the cross-sectional analysis in baseline data. By using the data of 10 256 participants from Third National Health and Nutrition Examination Survey, Wilhelm-Leen also demonstrated that the odds of frailty were substantially higher in participants with CKD Stages 1–5 than in those without [28].

Longitudinal studies of the association between frailty and eGFR have previously only focussed on the baseline eGFR associated with the incidence of frailty. In two cohort studies involving old populations, it was found that lower cystatin C-based eGFR was associated with an increased risk of incident frailty [29, 30]. We did not find this association in our cohort, which may be due to lack of statistical power resulting from the moderate longitudinal GFR decline within a limited follow-up period. However, frailty and kidney function decline may have a bidirectional relationship. Frailty may also be a risk factor for kidney impairment, as evidenced by our study.

What then are the mechanisms that frailty contributes to the development of kidney impairments? (i) Inflammation, which is a key pathophysiological process of physical frailty, may contribute to the progression of kidney function decline by inducing the release of cytokines and adhesion molecules, which together contribute to T-cell adhesion and migration into the interstitium of the kidney, subsequently attracting pro-fibrotic factors and impairing kidney function [31, 32]. (ii) Frail subjects have higher sympathetic and lower parasympathetic modulation [33, 34], higher oxidative stress and levels [35], marked deoxyribonucleic acid damage [36] and shorter telomere length [37] that could contribute to premature aging, which may manifest as rapid decline of kidney function [38]. (iii) With the development of frailty, the angiotensin receptors change towards more expression of Ang II Type 1 receptors (AT1Rs) [39]. AT1R stimulation promotes mitochondrial damage and reactive oxygen species production, both of which in turn trigger age-related vascular changes predisposing to increased kidney function decline [38]. (iv) Endocrine dysregulations present in frail people including lower sex hormone levels [7] and insulin-like growth factor-1 [40, 41] have been implicated in the repair ability of senescent kidneys [38, 42]. In short, frailty, reflecting the pathological decline of multiple inter-related physiology organ systems, may integrate the overall effects of individual risk factors to contribute to kidney damage in the elderly individuals [43]. The results from the mixed-effect model further showed that subjects with baseline frail status had a faster eGFR decline of 1.70 mL/min/1.73 m^2 compared with robust subjects at baseline, over the 3-year study period. It indicates that frailty

accelerates the progression of kidney function by 57% each year, supposing the normal ageing of GFR decline is 1 mL/min/1.73 m^2/year. Actually, we found this acceleration was as high as 5.00 mL/min/1.73 m^2 in males and 2.97 mL/min/1.73 m^2 in those without HBP or DM. However, these results need to be validated in a larger cohort. Nevertheless, it would be very interesting to investigate the accumulation effect of frailty on GFR decline by following the cohort for a longer time and in subgroup populations. Several approaches have been investigated in clinical trials to reduce the prevalence or severity of frailty, such as exercise interventions and nutritional interventions [44–47]. Future research is needed to investigate whether the treatment of frailty could prevent the kidney from pathological decline.

The limitations of this study should be noted. First, as with other observational studies, ours cannot prove causality. Secondly, GFR was estimated by the creatinine-based equation, which may be confounded by muscle mass. Given that the association could be found between frailty and rapid GFR decline even in the condition of overestimation of GFR level in subjects with low muscle mass, a stronger association may be established by alternative markers of glomerular filtration, such as cystatin C. Thirdly, potential selection bias may exist. However, the included population is a little younger and subsequently had higher GFRs, lower prevalence of COPD and higher uric acid, to a degree with limited clinical significance. In addition, our results may not be generalizable to other races and cohorts.

In conclusion, we found that baseline frailty was independently associated with the decline of kidney function in elderly people. Frailty may serve as an independent biomarker to predict early kidney function decline. Future studies are needed to explore whether prevention of kidney impairment in elderly populations would be benefit from improving frailty.

SUPPLEMENTARY DATA

Supplementary data are available at ndt online.

ACKNOWLEDGEMENTS

FUNDING

interpretation of data; writing the report; or the decision to submit the final report for publication.

AUTHORS' CONTRIBUTIONS

Research idea and study design carried out by M.W., X.S., X.W. and J.C. Data acquisition was done by M.W., W.Z., W.C., L.J., X.W. and J.C. Data analysis and interpretation were performed by M.W., W.Z., W.C., Q.Z., J.Q., S.Y., L.J., X.W., K.K.-Z. and J.C. Statistical analysis carried out by M.W., X.W. and J.C. Supervision or mentorship by X.W. and J.C.

DATA AVAILABILITY STATEMENT

J.C. and X.W. had access to all of the data in the study. Please contact these authors for data acquirement needs.

CONFLICT OF INTEREST STATEMENT

The authors declare that they have no relevant financial interests.

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