Original Article

Association between the combined effect of frailty and the estimated glomerular filtration rate and non-elective hospital readmission in elderly inpatients: a cohort study

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Background: This study aims to explore the combined effect of frailty and the estimated glomerular filtration rate (eGFR) and non-elective hospital readmission in elderly inpatients.

Methods: A total of 400 elderly patients were selected. The Fried scale was used to assess frailty. The patients were divided into a non-frailty group and a frailty group. They were divided into a normal eGFR group and a eGFR decreased group. Finally, the patients were divided into the following four groups: Group A (no frailty + eGFR normal); Group B (no frailty + eGFR decreased); Group C (frailty + eGFR normal); and Group D (frailty + eGFR decreased).

Results: The results of the follow-up survival analysis showed the non-elective hospital readmission within 6 months of discharge. Group A, Group B, Group C, and Group D had an incidence of 21%, 26%, 24%, and 36%, respectively. The Kaplan-Meier curves showed the event-free survival rates of Group A and Group C were higher than that of Group D, and there was no significant difference between Group B and Group D. The risk of non-elective hospital readmission within 6 months in patients with a decreased eGFR was 1.777 times higher than that in patients with a normal eGFR [95% confidence interval (CI): 1.001–3.154], while the risk of non-elective hospital readmission within 6 months in frail patients and non-frail patients did not differ significantly. The multivariate Cox regression analysis showed that the risk of non-elective hospital readmission in Group D was 2.295 times higher than that in Group A (95% CI: 1.096–4.810), and the difference was statistically significant. The risk of non-elective hospital readmission in Group B was 1.401 times of that in Group A (95% CI: 0.665–2.953), while that in Group C was 91.8% (95% CI: 0.403–2.092), but the differences were not statistically significant.

Conclusions: A decline in eGFR is associated with non-elective hospital readmission in elderly inpatients within 6 months; however, frailty is not associated with non-elective hospital readmission. The combined effect of frailty and eGFR in elderly inpatients is related to non-elective hospital readmission.

Keywords: Frailty; estimated glomerular filtration rate (eGFR); non-elective hospital readmission; combined effect

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Introduction

Frailty is one of the most common geriatric syndromes. As the elderly grow older, physical system degradation can lead to increased susceptibility to adverse health outcomes, such as falls, fractures, depression, and decreased health-related quality of life. Jiao *et al.* (1) found that the prevalence of frailty in elderly patients was 18.02% in 6 tertiary hospitals in China, and frailty was associated with age, body mass index (BMI), education background, and drinking history. Fan *et al.* (2) showed that frailty was associated with ischemic heart disease, cerebrovascular disease, and cancer, and the frailty index was associated with the all-cause mortality of Chinese residents. The prevalence rate of chronic kidney disease is 11.41% in China, which is associated with age, gender, diabetes, and hypertension, leading to a lower quality of life and increased medical expenses (3). Mei *et al.* (4) showed that frailty predicts negative outcomes in patients with chronic kidney disease, such as all-cause mortality, all-cause hospitalization, and falls. Suzuki *et al.* (5) found that estimated glomerular filtration rate (eGFR) variability in patients with chronic kidney disease can predict hospitalization and death due to cardiovascular factors. Frailty and decreased eGFR may have a synergistic effect on the prognosis of elderly patients; however, there are few studies on the combined effect of frailty and eGFR on the prognosis of elderly hospitalized patients. This study sought to explore the relationship between the combined effect of the 2 and the non-elective hospital readmission of elderly inpatients within 6 months. We present the following article in accordance with the STROBE reporting checklist (available at https://apm.amegroups.com/article/view/10.21037/apm-21-2327/rc).

Methods

Patients

A total of 400 elderly patients, aged 65 and above, were selected from September 2018 to December 2018 from 10 clinical departments of a Beijing hospital to participate in this prospective cohort study. Patients were excluded from the study if they met any of the following exclusion criteria: (I) could not cooperate with the examination and follow-up procedure; (II) had an advanced malignant tumor, and could not tolerate the test; (III) had a mental illness or another issue that meant they could not cooperate with the clinical trial; and (IV) did not undergo all the examinations and refused to participate in the follow-up examinations.

A total of 550 participants were included in our study, of whom 150 were excluded. Thus, ultimately, 400 were included in the study. No cases were lost during the follow-up period (thus, the follow-up rate was 100%).

All procedures performed in this study involving human participants were in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by ethics board of Beijing Hospital (No.: LLKYPJ: 2012041) and informed consent was taken from all the patients.

Study procedures

Clinical data collection and blood sample collection

Data on gender, age, and past history were collected, and patients' height and weight were measured. The diagnostic criteria for type 2 diabetes were based on the guidelines for the prevention and treatment of type 2 diabetes [2020]. The diagnostic criteria for hypertension were based on the guidelines for the prevention and treatment of hypertension [2019]. The diagnostic criterion for smoking was smoking for more than 6 months. The diagnostic criterion for drinking was cumulative drinking for more than 6 months. BMI was calculated as weight divided by height in meters squared. After fasting for 8 hours, 8 mL of blood was collected and sent to the laboratory within 2 hours to detect total bilirubin, creatinine, low density lipoprotein cholesterol, uric acid, lactate dehydrogenase, triglyceride, total protein, albumin, alanine aminotransferase, high-density lipoprotein cholesterol, aspartate aminotransferase, direct bilirubin, total cholesterol, and creatine kinase.

Diagnostic criteria for frailty

According to the frailty phenotype, frailty was defined as frailty with a score of ≥3, and non-frailty was defined as frailty with a score of ≤2 (6). The frailty phenotype was assessed by 2 standardized testers.

Diagnostic criteria for the decreased eGFR in the elderly

The eGFR was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula. An eGFR <60 mL/min/1.73 m^2 was defined as a decreased eGFR, and an eGFR ≥60 mL/min/1.73 m^2 was defined as a normal eGFR.

Follow-up data collection

Within 6 months of discharge, outpatient follow-up, telephone follow-up, and in-hospital follow-up examinations were conducted. The endpoint was defined as non-elective hospital readmission, including the aggravation of disease and hospitalization recommended by community doctors..

Cut off values in groups

Based on their Fried scores, the patient was divided into the 2 following groups: (I) the non-frail group (n=282, Fried ≤2); and (II) the frail group (n=118, Fried ≥3). A Cox regression analysis was conducted to analyze the relationship between frailty and non-elective hospital readmission.

Based on their eGFR, the patients were divided into the following 2 groups: (I) the normal eGFR group (n=280, eGFR ≥60 mL/min/1.73 m^2); and (II) the decreased eGFR group (n=120, eGFR <60 mL/min/1.73 m^2). A Cox regression analysis was conducted to analyze the relationship between eGFR and non-elective hospital readmission.

Based on their Fried score and eGFR, the patients were divided into the following 4 groups: (I) Group A (n=212, no frailty + normal eGFR); (II) Group B (n=70, no frailty + decreased eGFR); (III) Group C (n=68, frailty + normal eGFR); and (IV) Group D (n=50, frailty + decreased eGFR). The association between the combined effect of frailty and eGFR on non-elective hospital readmission was analyzed by Cox regression.

Statistical analysis

SPSS 22.0 software was used for the statistical analysis. Mean ± standard deviation ($\bar{x}$±s) are used to describe the quantitative data with a normal distribution. A 1-way analysis of variance was used to compare the groups. Least significant difference *t*-tests were used for further pairwise comparisons. The median and interquartile distance [M (P_{25}–P_{75})] are used to express the quantitative data with a non-positive distribution. The Kruskal-Wallis *H* was used to compare the groups. The qualitative data were compared between groups by χ^2 tests. Next, Kaplan-Meier curves were drawn, and log-rank tests were used to compare differences in adverse prognoses among the different groups. The Cox proportional hazards regression model was used to analyze the risk of adverse prognoses of different groups after adjusting for other variables.

Results

Comparison of the general information of the 4 groups

A total of 400 patients were enrolled in the study, including 248 (62%) male patients, 118 (29.5%) frail patients, and 120 (30%) patients with a decreased eGFR. There were significant differences in age, creatinine, total protein, albumin, uric acid, total bilirubin, lactate dehydrogenase, alanine aminotransferase, total cholesterol, low density lipoprotein cholesterol, and hypertension among the different groups (P<0.05; see *Table 1*).

Follow-up survival analysis

A total of 97 participants had a non-elective hospital readmission during the 6-month follow-up period post-discharge. Group A, Group B, Group C, and Group D had an incidence of 21% (45/212), 26% (18/70), 24% (16/68), and 36% (18/50), respectively. The Kaplan-Meier curves showed the same trend (see *Figure 1*) (overall χ^2=11.213; P=0.011). The event-free survival rates of Group A (χ^2=10.398; P=0.0001) and Group C (χ^2=5.876; P=0.015) were higher than that of Group D, but there was no significant difference between Group B and Group D (χ^2=2.208; P=0.137).

Association between a decreased eGFR and non-elective hospital readmission within 6 months in elderly inpatients

Participants were divided into a normal eGFR group (n=280, eGFR ≥60 mL/min/1.73 m^2) and a decreased eGFR group (n=120, eGFR <60 mL/min/1.73 m^2). The relationship between eGFR and non-elective hospital readmission was analyzed by Cox regression. The results suggest that after adjusting for confounding factors, a decreased eGFR in elderly inpatients was associated with non-elective hospital readmission within 6 months. The risk of non-elective hospital readmission within 6 months in patients with a decreased eGFR was 1.777 times higher than that in patients with a normal eGFR [95% confidence interval (CI): 1.001–3.154] (see *Table 2*).

The association between frailty and non-elective hospital readmission within 6 months in elderly inpatients

Based on their Fried phenotype, patients were divided into a non-frail group (n=282, Fried score ≤2) and a frail group (n=118, fried ≥3). A Cox regression was used to analyze

Table 1 Comparison of the general information of the 4 patient groups

Variable	Group A (n=212)	Group B (n=70)	Group C (n=68)	Group D (n=50)	P
Age (years)	74.24±6.53	78.34±6.10[a]	77.40±6.49[a]	82.14±6.37[abc]	<0.001
Female, n (%)	132 (62.3)	38 (54.3)	48 (70.6)	30 (60.0)	0.263
Smoking, n (%)	140 (66.0)	50 (71.4)	43 (63.2)	32 (64.0)	0.745
Drinking, n (%)	124 (58.5)	45 (64.3)	44 (64.7)	32 (64.0)	0.693
BMI (kg/m^2)	25.20±3.31	24.71±3.12	24.50±3.17	24.59±3.36	0.329
Scr (μmol/L)	71.50 (59.00, 89.00)	113.00 (104.75, 124.50)[a]	68.00 (56.25, 91.00)[b]	116.50 (104.75, 172.75)[ac]	<0.001
TP (g/L)	66.24±5.45	67.16±5.56	65.51±6.29	64.34±5.98[ab]	0.047
Alb (g/L)	39.57±3.09	38.93±3.32	38.57±4.08[a]	37.48±3.22[ab]	0.001
Uric (μmol/L)	342.00 (269.50, 408.75)	393.50 (337.25, 500.25)[a]	351.50 (265.00, 428.25)[b]	386.50 (332.00, 474.50)[a]	<0.001
TBiL (μmol/L)	11.05 (8.33, 14.70)	10.10 (7.98, 13.75)	11.50 (8.93, 14.00)	8.75 (6.98, 11.20)[ac]	0.001
DBiL (μmol/L)	3.90 (3.10, 5.50)	3.95 (2.80, 5.13)	4.55 (3.40, 5.60)	3.75 (2.70, 4.85)	0.091
AST (U/L)	22.01±11.07	22.31±13.34	23.73±15.53	20.86±10.35	0.635
LD (U/L)	175.03±38.69	184.79±46.57	191.63±41.78[a]	195.21±68.88[a]	0.006
CK (U/L)	83.50 (61.00, 108.00)	80.00 (51.00, 142.25)	72.25 (55.50, 112.50)	64.50 (43.75, 93.50)[a]	0.047
ALT (U/L)	16.00 (12, 22.75)	13.50 (11.00, 18.00)	15.00 (11.24, 25.00)	11.00 (9.00, 16.00)[ac]	<0.001
TC	4.00±0.99	3.94±0.90	3.54±0.85[ab]	3.69±0.86[a]	0.003
TG	1.36±0.9	1.41±0.79	1.17±0.81	1.23±0.54	0.235
HDL-C	1.10±0.27	1.02±0.21	1.06±0.28	1.02±0.20	0.059
LDL-C	2.40±0.77	2.41±0.72	2.04±0.62[ab]	2.22±0.80	0.003
HBP, n (%)	137 (64.6)	61 (87.1)[a]	51 (75.0)	42 (84.0)[a]	<0.001
DM, n (%)	61 (28.8)	29 (41.4)	30 (44.1)	19 (38.0)	0.056
CHD, n%	120 (56.6)	33 (47.1)	35 (51.5)	27 (54.0)	0.559
Stroke, n (%)	46 (21.7)	10 (14.3)	20 (29.4)	16 (32.0)	0.070

[a], compared with Group A, P<0.05; [b], compared with Group B, P<0.05; [c], compared with Group C, P<0.05. The participants in Group A had a normal eGFR without frailty; the participants in Group B had a decreased eGFR without frailty; the participants in Group C had a normal eGFR and frailty; the participants in Group D had a decreased eGFR and frailty. BMI, body mass index; Scr, creatinine; TP, total protein; ALB, albumin; TC, total cholesterol; Uric acid, blood uric acid; TBIL, total bilirubin; TG, triglyceride; ALT, alanine aminotransferase; LDL-C, low density lipoprotein; DBIL, direct bilirubin; AST, glutamic oxaloacetic transaminase; LD, lactate dehydrogenase; HDL-C, high-density lipoprotein cholesterol; CK, creatine kinase. DM, diabetes mellitus; HBP, hypertension; CHD, coronary heart disease; eGFR, estimated glomerular filtration rate.

the association between frailty and non-elective hospital readmission. The results suggested that after adjusting for confounding factors, frailty was not associated with non-elective hospital readmission within 6 months. There was no significant difference in the risk of non-elective hospital readmission within 6 months between frail patients and non-frail patients (see *Table 2*).

Association of frailty and decreased eGFR with non-elective hospital readmission within 6 months in elderly inpatients

Then, based on their Fried phenotype and eGFR, the patients were divided into the following four groups: (I) Group A (n=212, no frailty + normal eGFR); (II) Group B (n=70, no frailty + decreased eGFR); (III) Group C (n=68,

frailty + normal eGFR); (IV) Group D (n=50, frailty + decreased eGFR). A multivariate Cox regression analysis was used to analyze the relationship between the combined effect of frailty and the eGFR and non-elective hospital readmission. The results showed that after adjusting for age, gender, smoking, uric acid, triglyceride, high-density lipoprotein, diabetes, and coronary heart disease, Group A was the reference group. The risk of re hospitalization in Group D was 2.295 times that of Group A (95% CI: 1.096–4.810); the difference was statistically significant. The risk of non-elective hospital readmission in Group B was 1.401 times higher than that in Group A (95% CI: 0.665–2.953), while that in Group C was 91.8% (95% CI: 0.403–2.092), but the difference was not statistically significant (see *Figure 2* and *Table 3*).

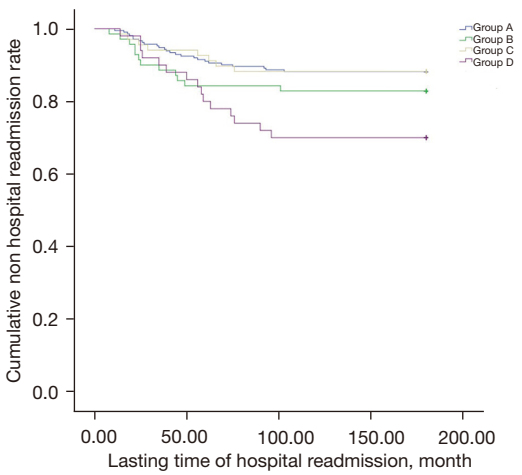

Figure 1 Overall χ^2=11.213; P=0.011; Group A was compared with Group B, χ^2=1.483; P=0.223; Group A was compared with Group C, χ^2=0.000; P=0.996; Group A was compared with Group D, χ^2=10.398; P=0.001; Group B was compared with Group C, χ^2=0.874; P=0.350; Group B was compared with Group D, χ^2=2.208; P=0.137; Group C was compared with Group D, χ^2=5.876; P=0.015.

Discussion

Certain factors may lead to a link between frailty and the eGFR. It is of great significance to explore the effects of related factors and prognosis on frailty and renal function in elderly patients. First, we divided the patients into an eGFR normal Group and an eGFR decreased group, and the results suggested that a decrease in eGFR was related to non-elective hospital readmission within 6 months. Next, patients were divided into a non-frail group and a frail group based on frail phenotype. Frailty was not associated with non-elective hospital readmission within 6 months. Finally, all participants were allocated to Group A (no frailty + normal eGFR), Group B (no frailty + decreased eGFR), Group C (frailty + normal eGFR), or Group D (frailty + decreased eGFR), and a multivariate Cox regression analysis showed that the combined effect of frailty and eGFR was associated with non-elective hospital readmission.

Frailty may be associated with the prognosis of elderly inpatients. Frailty refers to a decline in the physiological ability of multiple organ systems, which occurs with aging. In clinical and scientific research, the frailty index, the frail scale, clinical frailty scale and Edmonton frailty scale are used to evaluate the debilitating state of the elderly, among which the frailty index and fried are proved to be more accurate. The debilitation index includes 70 kinds of health defect items, including psychological, physiological, past history and other dimensions. It has been well verified in relevant studies such as health aging and Retirement Survey in Europe, but the calculation of debilitation index takes a lot of time and is not widely used in clinic. In the next study, the assessment of the debilitation index may be considered to be added to assess the debilitation status of the elderly.

Frailty increases the sensitivity to stressors, decreases

Table 2 Association of frailty and decreased eGFR with non-elective hospital readmission within 6 months

Variable	Unadjusted factors		Adjusted factors	
	HR (95% CI)	P	HR (95% CI)	P
Frailty[a]	1.507 (0.895–2.535)	0.123	1.240 (0.714–2.155)	0.445
eGFR[b]	2.025 (1.218–3.368)	0.007	1.777 (1.001–3.154)	0.049

[a], the adjusted factors were age, gender, smoking, uric acid, triglyceride, high-density lipoprotein, diabetes, coronary heart disease, and eGFR abnormalities; [b], the adjusted factors were age, gender, smoking, uric acid, triglyceride, high-density lipoprotein, diabetes, coronary heart disease, and frailty. eGFR, estimated glomerular filtration rate; CI, confidence interval.

the quality of life, and gradually increases demands for a pension and medical care. Morton *et al.* (7) found that severe frailty [a clinical frailty scale (CSF)-09 score of 7–9] was independently associated with an increased risk of death within 2 weeks in 164 patients with acute hospitalization, and that severe frailty led to an increase in mortality within 1 year of acute admission (8). In the present study, patients were divided into a non-frail group and a frail group based on their frail phenotype. A multivariate Cox regression showed that frailty was not associated with non-elective hospital readmission within 6 months. There are a number of possible reasons for the differences between our results and those of previous studies. First, the follow-up time in the present study was short. Second, the number of cases in this study was small, and the selection of research objects was different. Specifically, we excluded some patients who could not tolerate the long-term evaluations, which may have led to the absence of some cases of severe frailty and affected the accuracy of the research results. As the Fried phenotype is widely used to assess frailty in elderly hospitalized participants (6), we chose the Fried phenotype for our study.

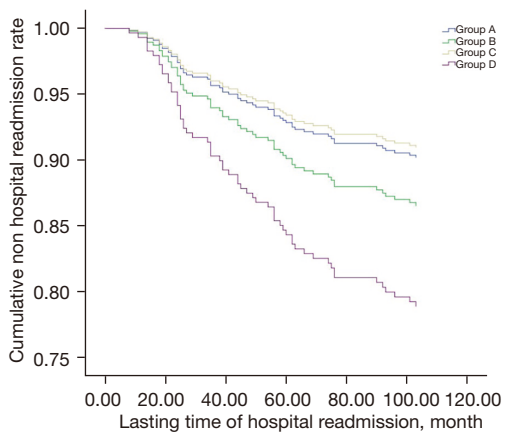

Figure 2 The adjusted factors were age, gender, smoking, uric acid, triglyceride, high-density lipoprotein, diabetes, and coronary heart disease.

In recent years, studies have shown that renal dysfunction is associated with the prognosis of patients. Kai *et al.* (9) showed that a low eGFR was associated with the prognosis of hemorrhagic stroke. Li *et al.* (10) showed that the eGFR was associated with in-hospital mortality. In our study, patients were divided into a normal eGFR group and a decreased eGFR group. The results of the multivariate Cox regression suggested that eGFR was associated with non-elective hospital readmission within 6 months. However, different conclusions have been drawn by others. For example, Ito *et al.* (11) found that in the eGFR reduction group, the eGFR of participants with proteinuria continued to decline after 4 years, while the eGFR of participants without proteinuria did not change significantly. Future studies may wish to detect the amount of urinary protein of participants, and then analyze the relationship between urinary protein and the non-elective hospital readmission of elderly inpatients.

The combination of the eGFR and frailty has rarely been studied in elderly patients. Chao *et al.* (12) found that frailty increased the risk of end-stage renal disease and death in 165,461 patients. Lee *et al.* (13) found that the prevalence of frailty in dialysis patients was 46%, and that age, being female, and diabetes were associated with an increased risk of frailty. Adame Perez *et al.* (14) found that chronic kidney disease, diabetes and adult frailty are associated with low lean weight, low quality of life, depression, and more medical visits. Sgambat *et al.* (15) found that the weak phenotype of 557 children with chronic kidney disease was associated with infection, hospitalization, and other adverse

Table 3 Association between the combined effect of frailty and decreased eGFR and non-elective hospital readmission within 6 months in elderly inpatients

Variable	Unadjusted factors		Adjusted factors[c]	
	HR (95% CI)	P	HR (95% CI)	P
Group A	1		1	
Group B	1.535 (0.771–3.056)	0.222	1.401 (0.665–2.953)	0.376
Group C	0.998 (0.450–2.212)	0.996	0.918 (0.403–2.092)	0.839
Group D	2.717 (1.432–5.154)	0.002	2.295 (1.096–4.810)	0.028

[c], the adjusted factors were age, gender, smoking, uric acid, triglyceride, high-density lipoprotein, diabetes, and coronary heart disease. eGFR, estimated glomerular filtration rate; CI, confidence interval.

outcomes. Our study suggests that the combined effect of frailty and a decreased eGFR in elderly inpatients is related to non-elective hospital readmission, and they may have a combined synergistic effect. Thus, the combination of frailty and the eGFR in the prognosis of elderly inpatients may be of significance to improve the quality of life of patients and reduce medical costs.

At present, the combined effect of frailty and eGFR has not received sufficient attention. Intervention methods for frailty include improving nutritional status, supplementing vitamin D, rehabilitation exercises, and multidisciplinary team interventions (16). Vettoretti *et al.* (17) used the frailty phenotype to evaluate the frailty status of 112 elderly patients with chronic kidney disease before dialysis, and found that it was helpful in identifying elderly patients with chronic kidney disease who may benefit from comprehensive assessments. Moffatt *et al.* (18) conducted semi-structured interviews with nurses, who suggested that frailty screening should be implemented in elderly patients with chronic kidney disease. The combined assessment of frailty and the eGFR was used in this study to explore the association between frailty and the eGFR and non-elective hospital readmission in elderly patients aged over 65 years.

Limitations

This research had some limitations. First, all the patients were from a Beijing hospital; thus, this is a single-center prospective cohort study, and the sample representation may be insufficient. In the future, a multicenter study should be conducted. Second, the sample size was small. Third, the Fried phenotype was used to evaluate frailty. This phenotype is mostly used for clinical and scientific frailty assessments, but the relatively simple content of the scale may have led to some biases. Fourth, due to the limited conditions, the quantitative detection of urinary protein was not carried out, and further research needs to be conducted to examine the relationship between the quantitative detection of urinary protein and the non-elective hospital readmission of elderly patients. Fifth, the follow-up time was short, and the risk of non-elective hospital readmission may be different before and after 6 months. Finally, non-elective hospital readmission was used as the endpoint event; however, some patients may have elected not to be rehospitalized for economic and social reasons, which may have led to the biases in the non-elective hospital readmission rate.

Conclusions

A low eGFR is associated with non-elective hospital readmission in elderly inpatients within 6 months; however, frailty is not associated with non-elective hospital readmission. The combined effect of frailty and eGFR in elderly inpatients is related to non-elective hospital readmission.

Acknowledgments

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://apm.amegroups.com/article/view/10.21037/apm-21-2327/rc

Data Sharing Statement: Available at https://apm.amegroups.com/article/view/10.21037/apm-21-2327/dss

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://apm.amegroups.com/article/view/10.21037/apm-21-2327/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study involving human participants were in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by ethics board of Beijing Hospital (No. LLKYPJ: 2012041) and informed consent was taken from all the patients.

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