Frequency and risk factors of frailty in nondialyzable chronic kidney disease geriatric patients

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Background
Frailty is an additional clinical and economic burden in the setting of chronic kidney disease (CKD). In this study, we aimed to determine the frequency and the risk factors for the occurrence of frailty in nondialyzable CKD geriatric patients' (stages 3–4).

Patients and methods
We conducted a cross-sectional, analytical study, which included consecutive patients with CKD, who attended the Nephrology Unit of Assiut University Hospital from April 2017 to April 2020. The total number of cases is 77 (21 of the control group and 56 of the patient group). Geriatric patients with aged more than or equal to 60 years and CKD stages 3–4 nondialysis dependent patients were included. The patients will be followed-up for 1 year.

Results
In terms of the frequency of frailty in geriatric CKD patients, the present study showed that 14.3% of the nondialyzable geriatric CKD patients had frailty. Regarding the predictors of frailty, the present study showed that nondialysis patients with frailty had significantly lower hemoglobin, mean corpuscular volume, mean corpuscular hemoglobin, platelet count, lymphocyte count, monocyte count, higher blood urea, higher serum creatinine, and higher basophil count. Notably, a lower serum magnesium level was noticed in the frail group.

Conclusion
In conclusion, frailty is not common in geriatric nondialysis dependent CKD patients. Independent risk factors for frailty in CKD include low serum magnesium and high serum creatinine.

Keywords:
chronic kidney disease, frailty, nerve conduction velocity

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Introduction

Chronic kidney disease (CKD) is defined as a persistent deterioration in kidney structure, function, or both for more than 3 months [1]. The condition is a global health burden with an estimated prevalence of 7–12% of the population worldwide [2]. In low-income and middle-income countries, the prevalence of CKD seems to be higher with reported rates of 10–16% according to pervious epidemiological figures [3]. CKD is a major debilitating disorder that may lead to a wide range of complications including cardiovascular diseases, metabolic acidosis, and hematological complications [4]. On the basis of the 2012 Classification of the Kidney Disease Improving Global Outcomes (KDIGO) [1], the CKD is classified into five stages according to the levels of glomerular filtration rate and albuminuria; end-stage renal disease (ESRD) is the final stage of CKD that is characterized by irreversible kidney damage that necessitates renal replacement therapy for survival [5].

ESRD is a major public health concern with a dramatic increase in its incidence rates over the past few decades owing to the increased longevity of the population and the epidemic of diabetes [6]. Patients with ESRD are at an increased risk of death and cardiovascular complications [7]; moreover, it was reported that ESRD is associated with reduced quality of life and depressive disorders [8]. On the other hand, ESRD represents an economic burden, especially for low-income and middle-income countries; patients with ESRD required frequent hospitalization and weekly hemodialysis treatment, which increase health-care expenditure for patients and providers [9]. Therefore, early prevention and proper management of CKD is an essential public health goal, for both patients and the society, to avoid the long-term consequences of ESRD [1].

Frailty is an age-related disorder that is characterized by progressive, unintentional weight and muscle

loss, in combination with generalized weakness and impaired physical function [10]. Frailty is associated with the occurrence of sarcopenia, which is a common, deleterious, adverse event of CKD, especially among patients with advanced stages of CKD; previous reports demonstrated that up to 40% of the dialysis patients are affected by sarcopenia [11]. Frailty can significantly impair the health status of CKD patients, where patients with frailty exhibited increased risks of osteopenia, falls and fracture, cardiovascular morbidity, impaired daily activity, disability, and death [12,13]. Thus, frailty is an additional clinical and economic burden in the setting of CKD. Various risk factors were implicated in the development of frailty including diabetes, ESRD, malnutrition, and BMI [14].

In this study, we aimed to determine the frequency of frailty in the nondialysis dependent CKD geriatric patients (stages 3–4). In addition, we aimed to determine the risk factors for the occurrence of frailty in those patients.

Patients and methods

The present study was approved by the local ethics and research committee of Assiut University Hospital with approval number (17101057). A written informed consent was obtained from every eligible patient before study enrollment.

Study design, setting, and patients

We conducted a cross-sectional, analytical study, which included all consecutive patients with CKD, who attended to the Nephrology Unit of Assiut University Hospital from April 2017 to April 2020. Geriatric nondialysis dependent CKD (stages 3–4) patients were included. The diagnosis of CKD was done according to the persistent deterioration in kidney function (CFR <60 ml/min/1.73 m^2 or albuminuria ≥30 mg/24 h) for more than 3 months. We excluded patients with a history of acute infection 1 month before study's enrollment, history of malignancy, history of active/chronic liver disease, history of autoimmune diseases, and patients who refused to sign the informed consent. A nonprobability consecutive sampling technique was used to recruit eligible patients

Data collection and measurement of CD molecule expression

We collected the following data from every participant: demographic characteristics, anthropometric measures, cause and duration of CKD, routine laboratory investigations, electromyography, and nerve conduction study.

Anthropometric assessment of the patients included weight, height, BMI (calculated as weight in kg divided by height in squared meters), and mid-arm muscle circumference (MAMC), which was calculated based on mid-arm circumference and the tricep skinfold using the following formula: MAMC = mid-arm circumference–(3.1415 × tricep skinfold) [15].

The electromyography study was applied to deltoid and tibialis anterior muscles. The muscle strength was assessed according to grip strength as measured by a dynamometer (MCZ-5041; Macros, Tokyo, Japan). The nerve conduction study was applied to the median, ulnar, tibial, and peroneal nerves to assess the latency, amplitude, and velocities of those nerves.

Fried's criteria for the diagnosis of frailty [13]:
(1) Involuntary weight loss.
(2) Weakness.
(3) Fatigue.
(4) Slowness.
(5) Decreased activity.

Measurements

Frail: more than or equal to 3 criteria.
Prefrail: 1–2.
No frail: 0.

Study's outcomes

The primary outcome in the present study was the frequency of frailty among geriatric nondialysis patients with CKD. The diagnosis of frailty was based on the presence of more than or equal to 3 Fried's criteria, which include involuntary weight loss, weakness, fatigue, slowness, and decreased activity.

Weakness was diagnosed by the presence of combination of low handgrip strength and low muscle quantity. Low handgrip strength was defined as less than 27 kg for males and less than 16 kg for females.

Statistical analysis

Data was collected and analyzed using SPSS (Statistical Package for the Social Sciences, version 20; IBM, Armonk, New York, USA). Continuous data was expressed in the form of mean ± SD or median (range), while nominal data was expressed in the form of frequency (percentage).

χ^2 test was used to compare the nominal data of different groups in the study while Student's t test was used to compare the mean of two different groups. Person's

correlation and other continuous variables were used. *P* value was significant if less than 0.05.

Results

The present cross-sectional, hospital-based, analytic study included 56 geriatric patients with CKD after exclusion of those with the exclusion criteria and 21 controls that were recruited from Assiut University Hospital. In terms of frequency of frailty in CKD, the present study showed that 14.3% of the patients with nondialyzable CKD had frailty (Fig. 1).

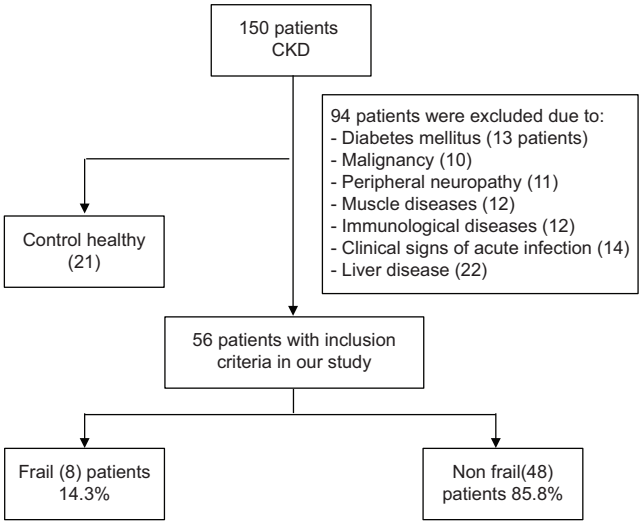
The mean age of the included patients was 71.45 ± 10.09 years and the majority of patients were males (89.3%). There were statistically significant differences between CKD patients and control group in terms of age (P = 0.046), sex (P = 0.006), MAMC (P = 0.011), systolic blood pressure (P = 0.007), and diastolic blood pressure (P = 0.001). In addition, patients with CKD had significantly more impairments in median nerve conduction velocity, ulnar nerve distal motor latency, and amplitude as well as amplitude and nerve conduction velocity of the deep peroneal nerve (P < 0.05). There is also significant difference in sensory nerve conduction velocity of the median nerve between the two groups. On the contrary, there were no significant differences between patients and control groups in other parameters. Table 1 shows the characteristics of CKD patients and the control group.

Among the CKD group, there were estatistically significant differences between frail-CKD and nonfrail-CKD patients in terms of sex (P = 0.024), BMI (P = 0.041), hemoglobin (P = 0.016), mean corpuscular volume (MCV) (P = 0.004), mean corpuscular hemoglobin (MCH) (P < 0.001), platelet (P = 0.029), albumin level (P = 0.001), serum creatinine (P = 0.012), urea (P = 0.04), and potassium levels (P = 0.022). On the contrary, there were no significant differences between frail-CKD and nonfrail-CKD patients regarding other parameters including calcium, phosphorus, and parathyroid hormone levels (Table 2).

Regarding the characteristics of the frail CKD patients versus the nonfrail CKD, the present study showed that the frail CKD patients had significantly higher frequency of occurrence of dementia, incontinence, more falls, and more skin breakdowns. In addition, frail CKD patients had significantly higher Charlson comorbidity index than nonfrail CKD patients (Table 3).

Interestingly, the univariate analysis showed that serum magnesium, MCV, and serum creatinine were independent associations of frailty (Table 4).

Figure 1



Flowchart of the results of the study.

Discussion

In this cross-sectional, observational study, we aimed to estimate the load of frailty in geriatric nondialyzable CKD patients.

Our results showed that 14.3% of the patients with nondialyzable CKD had frailty. Similar to our findings, a recent report in 2020 by Borges *et al.*[16] found that 33.2% of CKD nondialysis dependent patients had frailty. In this study, as a result of assessing the association between serum creatinine and frailty, the frequency of frailty increased as the creatinine level increases. The proportion of females was higher than the male proportion in the nonfrail group than those in the frail group. Though the mechanisms leading to frailty are not well understood, sex seems to have a serious effect on frailty occurrence, may be hormonal imbalance.

Regarding the clinical characteristics of frailty, the present study showed that frailty had a significant association with dementia. Our results were similar to Chang *et al.*[17] studies, which showed that about 20–55% of frail patients have cognitive impairment including dementia. Frailty and cognitive dysfunction tends to lessen the daily life activities and physical function [18].

Our study results observed no significant difference in other comorbidities, as the association of heart failure,

Table 1 Demographic, clinical, and nerve conduction study data of the studied groups

	Control group (*n*=21)	Patient group (*n*=56)	*P*
Age (years)	70.25±12.29	71.45±10.09	0.046
Sex (male/female)	61.9%/38.1%	89.3%/10.7%	0.006
Weight (kg)	69.83±9.49	65.63±7.2	0.076
Height (cm)	156.38±32.59	162.75±4.69	0.154
BMI	23.38±4.44	21.28±5.51	0.092
MAMC (cm)	19.71±1.72	23.19±4.35	0.011
MAC (cm)	23.07±1.85	25.36±6.05	0.095
SBP (mmHg)	129.52±12.44	139.29±15.71	0.007
DBP (mmHg)	69.05±5.39	74.82±7.13	0.001
MBP (mmHg)	91.42±9.05	96.48±9.56	0.038
Median. n lat (m/s)	3.44±0.4	4.24±0.77	0.073
M.n amp (mV)	14.22±4.11	10.71±4.63	0.117
M.n cv (m/s)	56.58±6.92	49.15±6.5	<0.001
Ulnar. n lat (m/s)	2.78±0.47	2.95±0.38	0.003
U.n amp (mV)	8.37±2.82	9.03±3.39	<0.001
U.n cv (m/s)	55.6±7.54	55.58±9.49	0.114
Posterior tibial n lat (m/s)	41.14±117.64	5±1.16	0.436
P.T. n amp (mv)	9.21±5.85	18.65±93.39	0.994
P.T. n cv (m/s)	53.38±7.29	39.38±5.58	0.023
Peroneal. n lat (m/s)	3.33±0.89	4.39±1.11	0.646
P .n amp (mv)	7.34±3.99	3.67±2.97	<0.001
P .n cv (m/s)	61.87±10.91	41.87±4.03	<0.001
Mean sensory NCV (Median .n) (m/s)	43.85±5.13	24.85±15.61	0.001
EMG (tibialis ant) amp (uv)	1100.48±429.85	914.73±387.33	0.174
Deltoid amp (uv)	1055.9±387.66	908.47±353.96	<0.001

Data are erpressed as mean±SD. DBP, diastolic blood pressure; DML, distal motor latency; EMG, electromyography; MAC, mid-arm circumference; MAMC, mid-arm muscle circumference; MBP, mean blood pressure; NCV, nerve conduction velocity; SBP, systolic blood pressure. *P*<0.05 is considered statistically significant.

Table 2 Laboratory parameters of frailty in geriatric nondialyzable chronic kidney disease

	Nonfrail (48) (85.8%)	Frail (8) (14.3%)	*P*
Sex (male/female). [*n* (%)]	9.1/90.9	80/20	0.024*
Age (years)	69.85±13.94	75.39±11.53	0.453
BMI (kg/m^2)	20.35±3.58	26.16±5.18	0.041*
HGB	10.97±1.18	9.25±1.12	0.016*
MCV (fl)	84.91±3.79	77.14±4.81	0.004**
MCH (pg)	27.96±1.57	23.57±0.53	<0.001**
PLT (10^3/μl)	240.45±76.23	171.29±28.33	0.029*
ALB (g/dl)	3.85±0.29	3.16±0.19	<0.001**
Urea (mmol/l)	31.12±7.35	40.93±9.57	0.040*
N (10^3/μl)	9.03±5.26	11.99±5.06	0.214
L (10^3/μl)	1.29±1.21	0.63±0.18	0.029*
B (10^3/μl)	0.25±0.25	2.77±2.53	<0.001**
M (10^3/μl)	1.56±2.22	0.4±0.37	0.034*
Creatinine (μmol/l)	8.4±1.2	10.6±2.2	0.012*
K (mmol/l)	4.9±0.8	6.1±1	0.022*
Ca (mg/dl)	8.25±1	8.6±1	0.527
P (mg/dl)	5.3±1.4	5±1	0.630
PTH (pg/ml)	269.3±386.6	274.8±296.55	0.978
Mg (mg/dl)	2.16±0.29	1.92±0.03	0.042*
CRP (mg/dl) [median (0.10-7.67)]	0.46 (0.10-3.19)	0.59 (0.1-7.67)	0.167

Data are expressed as mean±SD. B, basophil; Ca, calcium; CRP, C-reactive protein; HGB, hemoglobin; K, potassium; L, lymphocyte; M, monocyte; MCH, mean corpuscular hemoglobin; MCV, mean corpuscular volume; Mg, magnesium; N, neutrophil; P, phosphorus; PLT, platelet; PTH, parathyroid hormone. *P*<0.05 is considered statistically significant.

other cardiovascular diseases, and sleep disorders with frailty; still, the occurrence of frailty is considered to increase because of the accumulation of various comorbidities. These results were in contrast to Dogrul *et al*. [18], which showed that the increase in frailty frequency is associated with the presence of coronary syndrome and heart failure, which is eventually associated with readmission.

Table 3 Characteristics of all the studied patients with frailty status versus those without

	Nonfrail (48) (85.8%)	Frail (8) (14.3%)	*P*
Charlson Index (median)	6	7	0.01
Cardiovascular disease	8 (16.6)	1 (12.5)	0.44
Heart failure	12 (25)	2 (25)	0.453
Dementia	5 (10.5)	4 (50)	0.001**
Repeated falls	2 (4.7)	2 (11.42)	0.022*
Limitations to motility	4 (8.3)	5 (50)	0.001**
Sleep disorder	14 (29.16)	2 (25)	0.12
Incontinence	4 (8.33)	6 (75)	0.001**
Skin breakdown	1 (2.08)	2 (25)	0.001**

P<0.05 is considered statistically significant.

Table 4 Odds ratio for frailty in geriatric nondialyzable chronic kidney disease

	Univariate	
	OR (95% CI)	*P*
Age	73.981 (0)	0.994
BMI (kg/m^2)	1.075 (0.917-1.261)	0.372
PTH	1.002 (0.998-1.005)	0.393
Serum Mg	0 (0-0.073)	0.031*
CRP	0.46 (0.143-1.481)	0.193
HGB	1.527 (0.831-2.806)	0.173
ALB (g/dl)	0.021 (0-1.844)	0.091
MCV (fl)	0.658 (0.461-0.939)	0.021*
Creatinine (μmol/l)	0.997 (0.994-1)	0.048*

ALB, albumin; CRP, C-reactive protein; HGB, hemoglobin; MCV, mean corpuscular volume; Mg, magnesium; PTH, parathyroid hormone. *P*<0.05 is considered statistically significant.

Hubbard and Woodhouse[19] stated that there is an enormous relation between frailty and inflammation and he explained this relation by several mechanisms. The major one is mainly due to the catabolic effect of pro-inflammatory cytokines on muscles. The second mechanism is a reflection of the compensatory state of the frailty pathophysiology [20]. The third mechanism occurs due to unopposed and excessive oxidative stress. which may be the cornerstone in the development of age-related frailty [21]. These findings suggest that inflammation directly or indirectly plays a major role in the pathophysiology of frailty; thus, the finding in our study, which shows that nondialysis patients with frailty had a significantly lower MCV, MCH, platelet count, lymphocyte count, and monocyte count could be explained. Our important findings indicate the presence of a significant risk for frailty even within the normal range of total white blood cell in the CKD geriatric population. Interestingly, Veronese N *et al.*[22] showed that lower monocyte counts can significantly predict hospitalizations in frail geriatric patients, which is similar to our results where a lower monocyte count is associated with the occurrence of frailty in CKD geriatric nondialysis patients. It has been documented that frailty is associated with lower levels of various minerals, such as magnesium. Magnesium has a major part in the metabolism of the muscle where it is important for muscle movement [23]. Notably, serum magnesium and serum creatinine were independent associations of frailty. The exact causes of many risk factors for frailty in nondialysis geriatric CKD patients are largely unknown.

In concordance with our findings, Chia-Ming L *et al.*[24] reported that frailty was more prevalent in the more advanced stages of CKD and higher serum creatinine. Similarly, Lin *et al.*[25] showed that lower hemoglobin, platelet count, and higher serum creatinine were more frequent in frail geriatric patients. To date, no previous studies have assessed the role of hematological indices in frailty among nondialysis CKD geriatric patients. However, previous reports assessed the role of those parameters with sarcopenia in non-CKD patients [26].

In concordance with our results, Chao *et al.*[27] stated that frailty is complicated with several conditions in CKD patients, including cardiac disorders, musculoskeletal, metabolic, and nervous system disorders, which contribute to the morbidity and mortality in those patients.

In agreement with our results shown in Table 1, Jasti *et al.*[28] found that uremic neuropathy is the most common complication seen in CKD patients, which mainly present in the form of asymptomatic uremic neuropathy with enormous effect on the motor distal latency and motor conduction velocity and low motor amplitude. These findings could be explained by the segmental demyelination and axonal degeneration in peripheral nerves because of uremic toxins.

We acknowledge that the present study has a number of limitations. The study was cross-sectional in nature with a short follow-up of the included patients and therefore we could not study the change in the identified risk factors over long periods of time. Moreover, the study was conducted in one center only, which may affect the generalizability of our findings.

In conclusion, frailty is prevalent in 15% of CKD. Independent risk factors for frailty in nondialysis geriatric CKD patients include MCV, serum magnesium, and serum creatinine. These findings are very important as it confirms the need for interventions that aim to minimize risk factors that are recommended in geriatric CKD patients. Nevertheless, further studies with a rigorous design, a large sample size, and multiregional cooperation are required.

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Conflicts of interest
There are no conflicts of interest.

References

1 Stevens PE, Levin A. Evaluation and management of chronic kidney disease: synopsis of the kidney disease: Improving global outcomes 2012 clinical practice guideline. Ann Intern Med 2013; 158:825–830.

2 Zhang L, Wang F, Wang L, Wang W, Liu B, Liu J. Prevalence of chronic kidney disease in China: a cross-sectional survey. Lancet 2012; 379:815–822.

3 Shaheen FAM, Souqiyyeh MZ. Kidney health in the Middle East. Clin Nephrol 2010; 74(Suppl 1):S85–S88.

4 Jha V, Garcia-Garcia G, Iseki K, Li Z, Naicker S, Plattner B. Chronic kidney disease: global dimension and perspectives. Lancet 2013; 382:260–272.

5 Ruiz-Ortega M, Rayego-Mateos S, Lamas S, Ortiz A, Rodrigues-Diez RR. Targeting the progression of chronic kidney disease. Nat Rev Nephrol 2020; 16:269–288.

6 Narres M, Heiner C, Sigrid D, Tatjana K, Michael K, Oliver K. The incidence of end-stage renal disease in the diabetic (compared to the non-diabetic) population: a systematic review. PLoS ONE 2016; 11:e0147329.

7 Perneger TV, Klag MJ, Whelton PK. Cause of death in patients with end-stage renal disease: death certificates vs registry reports. Am J Public Health 1993; 83:1735–1738.

8 Spiegel BMR, Melmed G, Robbins S, Esrailian E. Biomarkers and health-related quality of life in end-stage renal disease: a systematic review. Clin J Am Soc Nephrol 2008; 3:1759–1768.

9 Wang V, Vilme H, Maciejewski ML, Boulware LE. The economic burden of chronic kidney disease and end-stage renal disease. Semin Nephrol 2016; 36:319–330.

10 Breccia M, Palandri F, Luciano L, Benevolo G, Bonifacio M, Caocci G, Lurlo A. Identification and assessment of frailty in older patients with chronic myeloid leukemia and myelofibrosis, and indications for tyrosine kinas inhibitor treatment. Ann Hematol 2018; 97:745–754.

11 Ortiz A, Sanchez-Niño MD. Sarcopenia in CKD: a roadmap from basic pathogenetic mechanisms to clinical trials. Clin Kidney J 2019; 12:110–112.

12 Clarke AL, Zaccardi F, Gould DW, Hull KL, Smith AC, Burton JO, Singh SJ. Association of self-reported physical function with survival in patients with chronic kidney disease. Clin Kidney J 2019; 12:122–128.

13 Bieniek J, Wilczynskil K, Szewieczek J. Fried frailty phenotype assessment components as applied to geriatric inpatients. Clin Interv Aging 2016; 11:453.

14 Chao C-T, Lee S-Y, Wang J, Chien K-L. Frailty increases the risk for developing urinary tract infection among 79,887 patients with diabetic mellitus and chronic kidney disease. BMC Geriatr 2021; 21:1–12.

15 Amador VAG, Freitas ERS, Peixto MdR. Anthropometric measurements and markers of renal function in adults and older adults. Rev Nutri 2016; 29:199–209.

16 Borges MK, M Canevelli, I Cesari. Frailty as a predictor of cognitive disorders: a systematic review and meta-analysis. Front Med 2019; 6:26.

17 Chang J, Gao Y, Fang XY, Zhao SM, Hou YP, Sun QM. Individualized intervention for frail non-dialysis elderly patients with chronic kidney disease: protocol for a randomized controlled trial. BMC Geriatr 2020; 20:1–8.

18 Dogrul RT, Varan HD, Cemel M, Kemal M. Relationship between frailty and inflammation. Euro J Geriatr Gerontol 2019; 1:17.

19 Hubbard RE, Woodhouse KW. Frailty, inflammation and the elderly. Biogerontology 2010; 11:635–641.

20 Sánchez-Garcia S, Sánchez-Arenas R, García-Peña C, Rosas-Carrasco O, Avila-Funes JA, Ruiz-Arregui L, Juárez-Cedillo T. Frailty among community-dwelling elderly Mexican people: prevalence and association with sociodemographic characteristics, health state and the use of health services. Geriatr Gerontol Int 2014; 14:395–402.

21 Fernansez-Garrido J, Ruiz-Ros V, Verdejo Y, Cauli O, Camps L. Frailty and leucocyte count are predictors of all-cause mortality and hospitalization length in non-demented institutionalized older women. Exp Gerontol 2018; 103:80–86.

22 Veronese N, B Stubbs, Ligia J, J Firth, S Maggi. Dietary magnesium and incident frailty in older people at risk for knee osteoarthritis: an eight-year longitudinal study. Nutrients 2017; 9:1253.

23 Chowdhury R, Peel NM, Hubbard RE. Frailty and chronic kidney disease: a systematic review. Arch Gerontol Geriatr 2017; 68:135–142.

24 Chia-Ming L, Chao C-T, Han D-S, Huang K-C. Elevated red cell distribution width is independently associated with a higher frailty risk among 2,932 community-dwelling older adults. Front Med 2020; 7:470.

25 Lin J, Zhang W, Huang Y, Chen W, Wu R, Chen X, P Wang. Sarcopenia is associated with the neutrophil/lymphocyte and platelet/lymphocyte ratios in operable gastric cancer patients: a prospective study. Cancer Manag Res 2018; 10:4935–4944.

26 Liaw FY, Huang CF, Chen WL, Wu LW, Peng TC, Chang YW. Higher platelet-to-lymphocyte ratio increased the risk of sarcopenia in the community-dwelling older adults. Sci Rep 2017; 7:16609.

27 Chao CT, Chiang CK, Huang JW, Kuan YH, J-W Huang. Selfreporte frailty among end-stage renal disease patients: a potential predictor of dialysis access outcomes. Nephrology 2017; 22:333–334.

28 Jasti DB, Vengamma SMB, Sivakumar V, Apparao A. A clinical and electrophysiological study of peripheral neuropathies in predialysis chronic kidney disease patients and relation of severity of peripheral neuropathy with degree of renal failure. J Neurosci Rural Pract 2017; 8:516–524.