Frailty has been widely recognised as a geriatric syndrome and emerging risk factor for adverse health outcomes in older adults. Frailty in older adults is linked to greater risk of falls, hospitalization, disability and death [1,2]. In Korea, reports indicated that the prevalence of frailty ranged from 2.5% to 31.7% depending on the study sample and frailty scale measure [3-5].

Frailty transitions and cognition among older adults:findings from the Korean Longitudinal study of Aging

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INTRODUCTION

- Frailty has been widely recognised as a geriatric syndrome and emerging risk factor for adverse health outcomes in older adults. Frailty in older adults is linked to greater risk of falls, hospitalization, disability and death.
- In Korea, reports indicated that the prevalence of frailty ranged from 2.5% to 31.7% depending on the study sample and frailty scale measure. Numerous studies have shown that frailty is of dynamic nature, demonstrating the changeability of frailty over time. Transitions in frailty status could be attributed to the fact that the concept of frailty is complex and multidimensional, with components derived from the social, physiological and physical phenotype.
- Cognitive impairment and dementia is a significant public health consequence in the aging demographic. Additionally, the relationship between the physical phenotype of frailty and cognitive function has been reported in countless studies, both cross-sectional and longitudinal.
- Therefore, based on these considerations, we investigated the effect of frailty transitions on cognitive function among older adults in South Korea.

MATERIALS AND METHODS

- **Data source**: Our present study extracted data over a 10 year-period from the 2nd to 7th wave (2008 to 2018) of the Korean Longitudinal study of Aging (KLoSA).
- **Study population**: Our study was carried out on data derived from the KLoSA on 6,024 respondents aged ≥45 years after exclusion of those with missing values.
- **Outcome variables**: Respondent's cognitive function was measured using the Korean version of the Mini-Mental State Examination (K-MMSE) score. The instrument consists of seven cognitive function categories including time orientation, spatial orientation, registration, attention and calculation, recall, language, and visual construction domains. These items make up a composite score of 30 points, with greater scores indicating higher cognitive function.
- **Interesting variables**: Transitions in frailty status were assessed by measuring changes in frailty criteria defined by the Frailty Instrument (FI). The Frailty Instrument captures the social, physiological and physical phenotype of frailty through the incorporation of 3 criteria: exhaustion, social isolation and weakness of grip strength.
- **Covariates:** Sociodemographic and health-related characteristics were all included as control variables. General characteristics included: gender, age, education level ,income level per month, marital status, and economic activity. Health-related variables included: smoking, drinking, BMI, physical activity, ADL , IADL limitations and number of chronic diseases.
- **Statistical analysis**: The sociodemographic and health-related characteristics of study participants were compared using ANOVA. The level of statistical significance was $p < 0.05$. Transitions in frailty and their relationship with cognitive function were investigated using Generalised Estimating Equations (GEE). All statistical analyses were conducted using SAS 9.4 software (SAS Inc., Cary, NC, USA).

RESULTS

Table 1. General characteristics of study population at baseline (2008→ 2010) (N=6,024)

Variables	Cognitive function (K-MMSE)									
	Male					Female				
	N	(%)	Mean	SD	P-value	N	(%)	Mean	SD	P-value
Total	**2,730**	**(100.0)**	26.9	3.7		**3,294**	**(100.0)**	25.4	4.9	
Frailty transitions (2008→ 2010)					<.0001					<.0001
Non-Frail →Non-Frail	2,342	(85.8)	27.6	2.9		2,602	(79.0)	26.5	3.8	
Frail →Non- Frail	102	(3.7)	24.5	5.1		203	(6.2)	23.1	5.4	
Non-Frail → Frail	191	(7.0)	23.6	4.8		278	(8.4)	21.4	5.9	
Frail →Frail	95	(3.5)	21.4	5.9		211	(6.4)	19.0	6.5	

- In Table 1, mean K-MMSE was highest for Non-Frail →Non-Frail group 27.6 (SD: 2.9), 24.5 (SD: 5.1) for Frail →Non- Frail group, 23.6 (SD: 4.8) for Non-Frail → Frail group, 21.4 (SD: 5.9) for Frail →Frail group. Likewise, in women, Non-Frail →Non-Frail group had the highest K-MMSE score at 26.5 (SD: 3.8), 23.1 (SD: 5.4) for Frail →Non- Frail group, 21.4 (SD: 5.9) for Non-Frail → Frail group, 19.0 (SD: 6.5) for Frail →Frail group.

Table 2. Association of frailty transitions and cognitive function

Variables	Cognitive function (K-MMSE)					
	Male			Female		
	ß	S.E	P-value	ß	SD	P-value
Frailty transitions						
Non-Frail → Non-Frail	Ref.			Ref.		
Frail →Non- Frail	-1.500	0.182	<.0001	-1.352	0.153	<.0001
Non-Frail → Frail	-1.937	0.178	<.0001	-1.808	0.154	<.0001
Frail → Frail	-3.426	0.286	<.0001	-3.286	0.251	<.0001

- In Table 2, respondents who experienced frailty transitions, namely those with ameliorating frailty, or those who developed frailty and whose frailty remained constant, were more likely to have a lower cognitive function, compared to those who were consistently non-frail.

	Cognitive function (K-MMSE)											
	Frailty transitions											
	Non-Frail → Non-Frail			Frail → Non-Frail			Non-Frail → Frail			Frail → Frail		
	ß	S.E	P-value	ß	S.E	P-value	ß	S.E	P-value	ß	S.E	P-value
Male												
Age												
45-54	Ref.			-1.466	0.751	0.051	-1.581	0.507	0.002	-3.559	1.225	0.004
55-64	Ref.			-3.813	1.063	0.0003	-0.624	1.110	0.574	7.638	1.641	<.0001
65≤	Ref.			-1.781	0.224	<.0001	-2.162	0.216	<.0001	**-3.562**	**0.327**	**<.0001**
ADL limitations												
Yes	Ref.			0.597	2.364	0.801	-3.224	2.359	0.172	-4.340	2.405	0.071
No	Ref.			-1.600	0.182	<.0001	-1.865	0.170	<.0001	-3.394	0.276	<.0001
IADL limitations												
Yes	Ref.			-2.387	0.690	0.0005	-2.488	0.736	0.001	**-3.905**	**0.887**	**<.0001**
No	Ref.			-1.429	0.176	<.0001	-1.811	0.171	<.0001	-3.263	0.278	<.0001
Number of Chronic diseases												
0	Ref.			-1.536	0.277	<.0001	-1.813	0.263	<.0001	**-3.569**	**0.436**	**<.0001**
1	Ref.			-1.601	0.295	<.0001	-1.860	0.262	<.0001	-3.462	0.479	<.0001
≥2	Ref.			-1.479	0.414	0.0004	-2.501	0.399	<.0001	-3.504	0.544	<.0001
Female												
Age												
45-54	Ref.			-1.357	0.508	0.483	-1.135	0.485	0.019	-0.522	0.582	0.370
55-64	Ref.			-1.036	0.264	<.0001	-1.368	0.263	<.0001	-2.756	0.606	<.0001
65≤	Ref.			-1.519	0.193	<.0001	-2.011	0.192	<.0001	**-3.210**	**0.277**	**<.0001**
ADL limitations												
Yes	Ref.			-2.799	1.474	0.058	-5.969	1.484	<.0001	**-7.032**	**1.247**	**<.0001**
No	Ref.			-1.376	0.155	<.0001	-1.719	0.152	<.0001	-3.182	0.257	<.0001
IADL limitations												
Yes	Ref.			6.625	0.334	<.0001	0.763	0.510	0.134	2.065	0.442	<.0001
No	Ref.			-1.323	0.155	<.0001	-1.652	0.155	<.0001	-3.320	0.270	<.0001
Number of Chronic diseases												
0	Ref.			-1.564	0.249	<.0001	-1.809	0.264	<.0001	-3.256	0.468	<.0001
1	Ref.			-1.149	0.257	<.0001	-1.793	0.248	<.0001	**-3.536**	**0.373**	**<.0001**
≥2	Ref.			-1.416	0.323	<.0001	-1.950	0.311	<.0001	-2.935	0.507	<.0001

*Adjusted for other covariates

RESULTS

- In Table 3, older age≥ 65 years ; in men b = - 3.562 (p-value: <0.0001), and women b = - 3.210 (p-value: <0.0001) , ADL disability; in women b = - 7.032 (p-value: <0.0001), IADL disability; in men b = - 3.905 (p-value: <0.0001) were more negatively and significantly associated with decline in cognitive function, especially in the "Frail → Frail" group.

Table 4.Interesting subgroup analysis of Frailty instrument components with cognitve function

Variables	Cognitive function (K-MMSE)					
	Male			Female		
	ß	S.E	P-value	ß	S.E	P-value
Change in exhaustion						
No→No	Ref.			Ref.		
Yes→No	-0.447	0.124	0.0003	-0.581	0.112	<.0001
No→Yes	-0.817	0.119	<.0001	-1.112	0.114	<.0001
Yes→Yes	**-1.983**	**0.259**	**<.0001**	**-1.948**	**0.198**	**<.0001**
Change in social isolation						
No→No	Ref.			Ref.		
Yes→No	-0.637	0.130	<.0001	-0.667	0.119	<.0001
No→Yes	-1.071	0.134	<.0001	-1.162	0.119	<.0001
Yes→Yes	**-1.697**	**0.170**	**<.0001**	**-1.986**	**0.161**	**<.0001**
Change in weakness of grip strength						
No→No	Ref.			Ref.		
Yes→No	-0.824	0.121	<.0001	-0.957	0.128	<.0001
No→Yes	-1.147	0.121	<.0001	-1.259	0.126	<.0001
Yes→Yes	**-2.416**	**0.206**	**<.0001**	**-2.220**	**0.199**	**<.0001**

*Adjusted for other covariates

- In Table 4, compared to the No →No group, the Yes→Yes group showed the lowest estimate for both men and women for change in exhaustion; b = -1.983 (p-value: <0.0001), b = - 1.948 (p-value: <0.0001) , social isolation; b = - 1.697 (p-value: <0.0001), b = - 1.986 (p-value: <0.0001), and weakness of grip strength; b = - 2.416 (p-value: <0.0001), b = -2.220 (p-value: <0.0001), respectively.

DISCUSSION

- Through our findings, we managed to confirm that respondents aged 45 years or older that experienced frailty changes had a significantly lower cognitive function than those who were continuously non-frail.
- Numerous observational studies showed that a chronological relationship between frailty, cognitive impairment existed. Prior evidence suggests that the pathways linked with frailty in older adults are similar to those that promote neurodegeneration, including chronic inflammation and oxidative stress, and consequent cognitive decline.
- The relationship between older age, frailty and cognitive impairment has long been postulated in prior studies. The highest cognitive decline in the oldest age group ≥ 65 years in our study is an expected finding supported by other studies, given the fact that both frailty and cognitive impairment are age-related syndromes.
- Our study's subgroup analysis of our variable of interest also showed that the unfavourable transitions in individual components of the frailty instrument impacted cognitive function negatively. Out of all the correlates, constant weakness of grip strength showed the greatest decrease in cognitive function in males and females alike.
- This finding coincides with studies that stated that grip strength is the most important predictor of cognitive decline out of all frailty domains. Self-reported exhaustion was also associated with lower K-MMSE scores, despite other studies reporting the opposite, that it did not significantly affect cognitive function.
- There were several limitations in our study. First, although the frailty instrument has been previously validated in the Korean population, the measure of frailty used in this study is relatively simple and not a universally used scale such as Frield's phenotype scale. Second, although we analysed our study's data longitudinally, we could not rule out reverse causality between frailty transitions and cognitive function.

CONCLUSION

- Our present study's findings suggested that undergoing changes in frailty changes, developing frailty or remaining frail negatively affected cognitive function in adults aged older than 45 years in South Korea.
- Through our study's results, it is suggestive to draw a conclusion that frailty status can be a predictor or indicator of future cognitive decline.
- Hence, the implication our findings may assist in developing intervention and policies to prevent frailty and future cognitive impairment in older adults.