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Short-term Changes of Frailty in Pre-maturely Aging Adults with Intellectual Disabilities

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Abstract:	Study purposes were to investigate short-term changes of frailty in adults, and to identify predictors of frailty and disability changes between baseline and the follow-up. A cohort study was conducted in 85 adults with intellectual disabilities (ID) in southern Taiwan. Variables of frailty phenotype, Barthel index, fall, comorbidity and hospitalization were measured at baseline and at 9-month follow-up. Descriptive, correlations and generalized linear model technique were used for data analysis. The percentages of frailty and pre-frail conditions were high at baseline. Improvement or deterioration on frailty was noticed in 37.6% of participants. Disability and comorbidity were significant predictors to changes in frailty, while severity of ID and frailty conditions were significant predictors to changes in disability.

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ABSTRACT

Study purposes were to investigate short-term changes of frailty in adults, and to identify predictors of frailty and disability changes between baseline and the follow-up. A cohort study was conducted in 85 adults with intellectual disabilities (ID) in southern Taiwan. Variables of frailty phenotype, Barthel index, fall, comorbidity and hospitalization were measured at baseline and at 9-month follow-up. Descriptive, correlations and generalized linear model technique were used for data analysis. The percentages of frailty and pre-frail conditions were high at baseline. Improvement or deterioration on frailty was noticed in 37.6% of participants. Disability and comorbidity were significant predictors to changes in frailty, while severity of ID and frailty conditions were significant predictors to changes in disability.

KEYWORDS: Intellectual Disabilities, frailty, disability

Background

Life expectancy has increased in the last two decades in adults diagnosed with intellectual disabilities (ID) (Coppus, 2013), although knowledge about aging influence on cognition, physical, psychological and social functions of adults with ID remains incomplete (Martin et al., 2018). According to current knowledge, the aging process has been found to start earlier in middle-aged adults with ID compared to healthy older adults (McKenzie et al., 2017). Frailty is a syndrome indicated by normal aging in the general population and in adults with ID (Brehmer & Weber, 2010; Dent et al., 2019), and is defined as a dynamic process of age-related decline in multiple domains of functions and health (Dent et al., 2019; Martin et al., 2018).

A measurement of physical phenotype developed by Fried and colleagues is widely used in the general older population and adults with ID (Bouillon et al., 2013; Evenhuis et al., 2012; Schoufour et al., 2017). The limitations of cognitive and physical abilities in adults with ID may influence accountability of self-report measures, thus trained healthcare staff who are familiar with adults with ID in residential facilities are suggested to collect data or administer tests (Hilgenkamp et al., 2011). The predictive, concurrent and convergent validity are tested in the relationships between frailty and mortality, activities of daily living (ADL), fall, hospitalization and replacement to nursing home, but no reliability data was reported (Bouillon et al., 2013). Five items are proposed to measure frailty phenotype including weight loss, exhaustion, physical activity, walk time and grip strength (Fried et al., 2001). The presence of three deficits and above is indicated for “frail” condition; one or two deficits is indicated for “pre-frail” condition; and no deficit is indicated for

“robust” condition (Fried et al., 2001).

Several attributes and consequences have identified their associations with frailty. Firstly, frailty is coexistent with disability and comorbidity in adults with ID (Brehmer & Weber, 2010；Evenhuis et al., 2012); secondly, the occurrence of frailty is correlated with advance of age (Brehmer & Weber, 2010；Evenhuis et al., 2012；McKenzie et al., 2017); and thirdly, frailty causes vulnerability to adverse outcomes such as decline of activities of daily living, risk for fall, hospitalization, admission of long-term care institution and mortality (Martin et al., 2018; McKenzie et al., 2016; Schoufour, Echteld, et al., 2015).

Prevalence rates of frailty vary widely depending on the use of instruments and populations. The prevalence rates of frailty measured by Fried’s frailty phenotype were 13% in Dutch adults with ID (Evenhuis et al., 2012; Schoufour et al., 2017). A Dutch study reported the prevalence rate of the pre-frail condition measured by Fried’s frailty phenotype was 60% in ID adults (Evenhuis et al., 2012; Schoufour et al., 2017). The prevalence rates of frailty measured by other tools were reported in a range between 17% and 28%, and prevalence rates of pre-frail condition ranged from16% to 21% in Austrian and Canadian adults with ID (Brehmer-Rinderer et al., 2013; Martin et al., 2018; McKenzie et al., 2015; McKenzie et al., 2016).

Two pitfalls are encountered in surveying the prevalence of frailty in older general populations and adults with ID. Firstly, the prevalence rates of frailty or pre-frail condition varied widely while used different tools with varied cut-off points (Bouillon et al., 2013; Ofori-Asenso et al., 2019; Schoufour et al., 2017); for example, simultaneous use of both frailty phenotype and

frailty indices in the same sample demonstrated a wide difference of frailty percentages (13% vs. 25%-62%); and secondly, the dynamic and complicated nature of frailty and its interaction with disability and comorbidity might influence the prevalence rates cross-time. It is noted that frailty condition could be changed in the short-term period. A previous study indicated 11.8% of non-frail and 18.2% of pre-frail adults with ID became worse after 6-12 months of follow-up, with approximately 35% of pre-frail and 37% of frail adults having improved their conditions (Martin et al., 2018). Therefore, the short-term changes on frailty and its relationship with disability have not yet been determined in pre-maturely aging adults with ID.

Knowledge related to short-term changes of frailty and the relationships with adverse outcomes in adults with ID remains indeterminate. The purposes of this study were to investigate short-term changes of frailty and to identify predictors of frailty and disability changes between baseline and the follow-up in Taiwanese adults with ID.

Methods

Study design, participants and recruitment

This study was a one-year cohort study. Data were collected from a convenience sample of 85 adults with ID living in Kaohsiung city, in southern Taiwan. Inclusion criteria were adults having a diagnosis of intellectual disabilities; having age more than 40 years; and receiving day-care or institutional services. One hundred and six adults were recruited based on inclusion criteria in eight institutions. Seven adults with serious emotional or behavioral problems or who were unable to complete the interviewing and tests were excluded at baseline. Fourteen adults dropped out on the

follow-up period due to hospitalization, change of willingness and change of placement. Eighty-five adults completed two-time measures with the mean follow-up period of 9 months.

Measurements

A questionnaire of individual characteristics was developed by researchers to obtain data regarding age, gender and severity of ID by diagnosis. Barthel Index assessed ADL that asked participants' ability to perform dressing, feeding, bathing, grooming, transfer, mobility, climbing stairs, bowel continence, bladder continence and toileting activities. The study defined disability as more than one deficit in ADL. Comorbidity indicated the presence of at least one disease among hypertension, arthritis or diabetes mellitus. Two items inquired whether participants had fall incident or overnight hospitalization event in the last three months respectively.

Frailty was measured by frailty phenotype, which included weight loss, exhaustion, physical activity, walk time and grip strength (Fried et al., 2001). Measuring items and scores were described as the following and in reference to previous studies (Chan et al, 2012; Chen et al., 2014; Fried et al., 2001): (1) Weight loss: inquiring about "whether you have unintentional weight loss more than three Kg within three months?" Answer "yes" was scored 1 point; "No" was rated as 0 point. (2) Exhaustion: inquiring about two questions adopted from the Center for Epidemiologic Studies (CES-D) "I felt that everything I did was an effort" or "I could not get going." with occurrence at least occasionally or frequently. Answer "yes" was scored 1 point and "No" rated as 0 point. (3) Low physical activity: participants were evaluated by the Taiwan International Physical Activity Questionnaire short form (Liu, 2014). Below 20% of weekly energy expenditure among all

participants was scored 1 point. Counterparts were rated as 0 points. (4) Slowness: six-meter gait speed test was used. Participants walked as fast as possible to complete the round-trip of a 3-meter distance and their walking time was measured. Scoring was justified by gender and body height (ie. men's body height > 173 cm, walking time ≥ 6 seconds; women's body height > 159 cm, walking time ≥ 6 seconds; both scored 1 point and counterparts scored 0 points). (5) Weakness: hand-grip strength test was used. Participants held a dynamometer TTM-YD (Tokyo, Japan) with their dominant hand for their best effort. The maximal value was counted from two measures of hand-grip strength tests. Scoring was justified by gender and body mass index (BMI) (ie. men's BMI >28.1, grip strength ≥ 32Kg; women's BMI >29.1, grip strength ≥ 21Kg; both scored 0 points and counterparts scored 1 point). An item scoring 1 point represented a deficit. Presence of three or more deficits indicated a frail condition; one or two deficits indicated a pre-frail condition; and no deficit indicated a robust condition (Chan et al., 2012; Fried et al., 2001).

Ethical consideration, data collection procedure and data analysis

The Institutional Review Board (IRB) approved the study (IRB-SV(I)-xxx8), and the researcher received informed consents from participants and their family members after disclosing the study information adhered to IRB policy. All participants volunteered without coercion.

All measurements were collected by researchers through in-person interviews to participants, and all tests were performed by participants themselves at their institutions. Uncertain answers for questionnaires were verified by staff and participants' medical records. It took approximately 25 minutes to complete the tests and questionnaires. Data were collected at baseline and the mean of 9-

month follow-up.

Statistical analyses were conducted in the IBM SPSS, version 20.0. Descriptive statistics were used to define distributions of individual characteristics and frailty scores. Pearson correlation tests were done in continuous variables such as Barthel scores, age and frailty scores at baseline; Spearman's rho correlation (ρ) tests were performed in rank order variables including levels of ADL, frailty condition and severity of ID at baseline; Phi correlation coefficient (ϕ) was computed between dummy variables such as fall, comorbidity and hospitalization at baseline that recoded as 1 (≥1) and 0 (0); while Generalized linear model was used to test a linear model with dependent variable of "frailty condition at baseline and the follow-up" or "Barthel scores at baseline and the follow-up" at multivariate analysis, respectively. Significant correlates were computed as independent variables including age, severity of ID, comorbidity and frailty condition or disability. A parsimonious model was selected based on criteria of non-collinearity, model fitness of Wald χ^2 test and optimal values of estimation parameters. A *p*-value <0.05 indicated statistical significance. Bonferroni correction was taken to reduce the risk of an inflated type I error caused by conducting multiple tests.

Results

Characteristics of participants

The average age of the participants was 48.9 (SD=6.8); over half of the participants were female; and nearly 32% of the participants had moderate level of severity (Table 1).

At baseline and the follow-up, means of Barthel scores were 88.1 ± 17.4 – 91.5 ± 15.6

separately; approximately 54% - 67% were independent in ADL. At the follow-up, 70.6% of adults with ID were stable in ADL but 4.7% became worse; 24.7% showed improvement in ADL. In comorbidity, 40 - 49 % of the participants had at least one disease among hypertension, arthritis and diabetes mellitus regardless at baseline or the follow-up. However, 8 adults (9%) with ID had increase in number of diseases. Nearly 19% - 21% of the participants had at least one fall incident within three months at two measuring times. Low percentages of the participants (1% - 2%) had ever been admitted to hospital in the previous three months. Comparing percentage changes between baseline and the follow-up, there were significant differences in variables of ADL and comorbidity (Table 1).

Short-term changes in frailty conditions

According to pre-determinant criteria of frailty phenotype, 23.5% of participants had frailty and 68.3% had pre-frail conditions at baseline. At the follow-up, 20.0% of participants had frailty and 70.6% had pre-frail conditions (Table 1). Fifty-three (62.4%) participants maintained stability in their conditions; 21.1% improved, and 16.5% become worse at the follow-up. There were significant changes in frailty conditions as compared between baseline and follow-up but the difference dismissed while adjusting the significance level by multiple pairwise comparisons (Table 1).

Relationships between frailty, disability, comorbidity, fall and hospitalization at baseline

Correlations results showed frailty scores were significantly correlated with Barthel scores, levels of ADL and severity of ID at baseline ($r=-0.29 – 0.24$, $p<.05$); Barthel scores were

significantly correlated with fall and severity of ID at baseline (r=-0.36 – -0.39, $p < .01$); dummy variables of comorbidity, fall and hospitalization were not significantly correlated (ϕ =0.17– 0.19, $p > .05$). Frailty condition classified as frail, pre-frail or robust was significantly correlated with Barthel scores and levels of ADL (r=-0.27 – -0.37, $p < .05$), but was not correlated with comorbidity, fall and hospitalization (r=-0.04 – 0.12, $p > .05$) at baseline (Table 2).

Prediction models of frailty and disability changes between baseline and the follow-up

Prediction model of changes of frailty between baseline and the follow-up indicated significant predictors of disability and comorbidity. Age and severity of ID were included in the model but they were not significant (Table 3). Severity of ID and frailty condition were significant predictors of disability between baseline and the follow-up. The predictive model of disability was composed of insignificant variables including age and comorbidity (Table 3).

Discussion

Characteristics of participants

The mean age of participants in this study was slightly younger than those in Canadian and Dutch studies (Martin et al., 2018; McKenzie et al., 2015; Schoufour et al., 2017). Equal proportions of gender were included in this study, similar to the Canadian and Dutch studies (Martin et al., 2018; McKenzie et al., 2016; Schoufour, Echteld, et al., 2015). Study participants had lower percentages of moderate ID impairments than those in previous studies (McKenzie et al., 2015; Schoufour et al., 2017). Overall, the characteristics of study participants were similar to previous studies and hence able to provide international comparisons.

Short-term changes in disability, comorbidity, fall and hospitalization

The percentages of disability in ADL were higher than the numbers (15%-29%) reported in frail older adults (Bouzón et al., 2017; Hyde et al., 2016; Papachristou et al., 2017; Theou et al., 2012). The difference may be more likely related to participants' characteristics or pre-maturely aging change rather than the definition of disability used in the study. Partly because our definition of disability in ADL was similar to the definition adopted in a Spanish study (Bouzón et al., 2017) but was different from the definition "at least one or two deficit in instrumental ADL" used in previous studies (Hyde et al., 2016; Theou et al., 2012). It is noteworthy that nearly one-quarter of the participants improved their disability in ADL that might have occurred due to the unknown effect of regular physical exercise or functional training activities at the study sites. This result is less frequently reported in ID study and demands further survey in the future.

Our study results indicated the percentages of comorbidity were different from the percentage reported in frail older adults in the U.S. (77.2%) and Canada (13%-25%) studies (Fried et al., 2004; Theou et al., 2012). The percentage difference may result from the loose definition of comorbidity used in this study that differed from the definition "two or more chronic diseases" used in previous studies (Fried et al., 2004; Theou et al., 2012). Compared to the number at baseline, comorbidity had significant changes due to an increase in diagnoses of chronic disease. This result was similar to an increase of comorbid condition within a three-year follow-up period in Dutch adults with ID (Schoufour et al., 2017).

The percentages of fall were slightly lower and the percentage decreased in the follow-up in

the study as different from 24%-25% of fall events or a slight increase in fall within the follow-up period reported in the Dutch study (Schoufour et al., 2017). The decrease of fall events is encouraging even the significance of change is dismissed while adjusting by Bonfferoni correction.

Very low percentages of overnight hospitalization were noticed either at baseline or the follow-up. The percentages of hospitalization were lower than the numbers (11%-20%) reported in in Dutch adults with ID (Schoufour et al., 2017) and in older adults (Bouzón et al., 2017; Zhu et al., 2016). Comparing baseline and follow-up, the percentage of hospitalization had no significant difference. These results might be explained by our subjects being younger with less numbers of chronic disease than in previous studies (Bouzón et al., 2017; Schoufour et al., 2017; Zhu et al., 2016).

Short-term changes in frailty conditions

At baseline and follow-up, the percentages of frail condition in the study were lower than 27% to 39% reported in Canadian and Dutch adults with ID (McKenzie et al., 2015; Schoufour, Mitnitski, et al., 2015) but higher than 9%-17% indicated in Austrian, Canadian and Dutch adults with ID (Brehmer & Weber, 2010; Martin et al., 2018; Schoufour et al., 2017). These comparisons should be cautiously interpreted because differences might be caused by different measurements of frailty. The study showed high percentage of pre-frail condition in Taiwanese adults with ID similar to the Dutch studies (Evenhuis et al., 2012; Schoufour et al., 2017), but the values were lower than the percentages reported in previous studies (12%–28%) (Brehmer & Weber, 2010; Martin et al., 2018; McKenzie et al., 2015; Schoufour, Mitnitski, et al., 2015). The change of frailty conditions

becomes borderline significance between baseline and follow-up resulting in approximately 20% of the adults having improved or worsened, even though 60% maintained their conditions. It supports the hypothesis "frailty is a transition" (Martin et al., 2018).

Adults with frail condition are not always frail and the condition could be reversible or improved, and visa versa (Hyde et al., 2016; Martin et al., 2018). Emphasis should be placed on the pre-frail condition, and our study found the percentage increased at follow-up thereby echoing the previous Canadian study (Martin et al., 2018); accordingly, it should be concerning for clinicians that pre-frail condition at baseline might signal an increasing risk of frailty deterioration and mortality (Martin et al., 2018).

Correlations between major variables at baseline

Significant correlates were reported in the study; variables of comorbidity, levels of ADL, severity of ID and frailty condition were significantly inter-correlated. These associations were similar to findings reported in the previous study (Schoufour, Mitnitski, et al., 2015). Variables of fall and hospitalization were not significantly associated with frailty scores or frailty condition; the results echo the Dutch study (Schoufour, Echteld, et al., 2015) but contrast to significant associations found in older adults (Zhu et al., 2016). The results should be interpreted carefully due to operational definitions of fall and hospitalization varying among studies. Further exploration in studies with larger sample sizes is recommended.

Prediction models of frailty and disability changes between baseline and the follow-up

Study results indicated disability in ADL and comorbidity as significant predictors of frailty

changes between baseline and the follow-up, and this is expected because frailty is overlapped and associated with disability and comorbidity as studies conducted in adults with ID or frail older adults have indicated (Fried et al., 2004; Schoufour, Mitnitski, et al., 2015; Theou et al., 2012); however, age and severity of ID were not significant predictors of frailty, but this appeared inconsistent with previous ID studies (Evenhuis et al., 2012; McKenzie et al., 2015; Schoufour, Mitnitski, et al., 2015). We suggest relationships between variables of age and severity of ID and changes of frailty scores need more study tests in pre-maturely aging adults with ID.

Frailty condition and severity of ID were significant predictors of disability changes between baseline and follow-up. The prediction of frailty condition to disability was similar to the findings in ID adults and frail older adults (Evenhuis et al., 2012; Papachristou et al., 2017; Schoufour et al., 2017). Severity of ID as the predictor of disability was less reported but consistent with correlation results in this study; however, combining severity of ID with insignificant variables of age and comorbidity deserves more evidence to validate the prediction results regarding disability in future studies.

Study strengths and limitations

To our knowledge, this is the first study in Taiwan, even in Far-eastern countries, that investigates short-term changes of frailty in middle-aged and elderly adults with ID. Another strength of this study is that it enables comparison of results with international studies by use of the frailty phenotype measure. Finally, frailty as a transitional phenomenon and its associations with disability in ADL, fall, comorbidity, and hospitalization were tested in pre-maturely aging adults

with ID with comparisons of hypotheses proposed in previous studies.

There are several limitations in this study. Firstly, a small convenience sample composed of pre-maturely aging adults might limit the generalizability of the results; secondly, some participants might have comorbid conditions more than hypertension, arthritis and diabetes mellitus that could cause bias to results of comorbidity, disability and frailty; and finally, frailty was measured by frailty phenotype that could possess underlying influence by the severity of ID and existing physical disability. Validation of frailty results by objective measures are recommended in future studies.

Conclusions

Pre-frail condition is more commonly detected than frail condition in pre-maturely aging adults with ID. Adults with pre-frail or frail conditions possibly experience change over a short-term period and are associated with comorbidity and disability. Implementing a bundle of care interventions in a timely manner for prevention of frailty or management of chronic disease and ADL function is recommended.

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Table 1 Individual characteristics, frailty, disability, comorbidity, fall and hospitalization a baseline and follow-up (*N*=85)

Variables	Baseline			Follow-up			χ^2	*p*
	M ± SD	n	%	M ± SD	n	%		
Age	48.9 ± 6.8							
Sex								
Male		41	48.2					
Female		44	51.8					
Severity of ID								
Mild		8	9.4					
Moderate		27	31.8					
Severe		28	32.9					
Profound		22	25.9					
Comorbidity							58.02	<.001*
0		51	60.0		43	50.6		
≥ 1		34	40.0		42	49.4		
Fall							6.02	.014
0		67	78.8		69	81.2		
≥ 1		18	21.2		16	18.8		
Hospitalization							1.00	.976
0		83	97.6		84	98.8		
≥ 1		2	2.4		1	1.2		
ADL[a]	88.1±17.4			91.5±15.6			31.68	<.001*
Severe		10	11.8		6	7.1		
Moderate		27	31.7		19	22.3		
Mild		2	2.4		3	3.5		
Independent		46	54.1		57	67.1		
Frailty score	1.9 ± 0.9			1.8 ± 1.1			11.07	.026
Robust		7	8.2		8	9.4		
Pre-frail		58	68.3		60	70.6		
Frail		20	23.5		17	20.0		

Note: [a]ADL: Barthel scores categorized as four levels: 4=independent (100), 3=mild (≥ 91), 2=moderate (61-90), 1=severe (≤ 60), re-categorized into two groups (independent/dependent) in χ^2 test. *p< .001 (Bonferroni correction, 0.05/5)

Table 2 Correlations between major variables at baseline

Variables	1	2	3	4	5	6	7	8
1.Frailty score [a]	–							
2.Barthel score [a]	-.38**	–						
3.Comorbidity [c]	-.24**	.05	–					
4.Fall [c]	.05	-.39**	.17	–				
5.Hospitalization [c]	.05	.11	.19	.11	–			
6.ADL [b]	-.29**	.88**	.04	-.32**	.14	–		
7.Frailty condition [b]	.90**	-.37**	-.19	.12	-.04	-.27*	–	
8.Severity of ID [b]	.24*	-.36**	-.30**	.14	-.04	-.43**	.15	–
9.Age [a]	-.09	-.03	.23*	.05	.08	-.04	-.08	.05

Note: [a] Pearson correlations: frailty score, Barthel score, age; [b] Spearman correlations: ADL, frailty condition, severity of ID; [c] Phi correlations: Comorbidity, fall, hospitalization.

[d] Comorbidity:0(0), ≥1(1); Fall: 0(0), ≥1(1); Hospitalization: 0(0), ≥1(1); ADL: independent (4), mild (3), moderate (2), severe (1); Frailty condition: robust (1), pre-frail (2), frail (3); Severity of ID: mild (1), moderate (2), severe (3), profound (4).

*p <.05, **p <.001

Table 3 Prediction models of frailty and disability changes

Variables	B (SE)	Wald χ^2	df	*p*	95% Wald CI	
					Lower	Upper
Model: Frailty score [a,b]	1.52 (0.17)	81.14	1	<.001**	1.19	1.85
Age	0.06 (0.15)	0.17	1	.677	-0.23	0.35
Severity of ID	-0.17 (0.16)	1.18	1	.277	-0.49	0.14
Disability-severe	1.19 (0.26)	21.19	1	<.001**	0.69	1.70
Disability-moderate	0.51 (0.17)	8.89	1	.003*	0.18	0.85
Disability-mild	0.18 (0.42)	0.17	1	.680	-0.66	1.01
Comorbidity	0.30 (0.15)	4.14	1	.042*	0.01	0.59
Model: Barthel score [a,c]	77.56(3.16)	603.39	1	<.001**	71.37	83.75
Age	-1.46 (2.39)	0.37	1	.542	-6.15	3.23
Severity of ID	10.17 (2.40)	17.93	1	<.001**	5.46	14.88
Frailty-robust	17.40 (4.62)	14.17	1	<.001**	8.34	26.47
Frailty-prefrail	10.95 (2.84)	14.88	1	<.001**	5.38	16.51
Comorbidity	-0.38 (2.39)	0.03	1	.872	-5.07	4.30

Note. [a]Generalized linear model with intercept included; Wald χ^2 statistics: hypothesis tests of estimated parameters.

[b]Dependent variable=Frailty score at baseline and follow-up, independent variables include age [dummy as 0 (< 50years old), 1 (≥ 50 years old) =reference], severity [dummy as 0 (mild/moderate), 1 (severe/profound) =reference], disability [categorized ADL as 4 (independent)=reference, 3 (mild), 2 (moderate), 1 (severe), comorbidity [dummy as 0 (absence), 1 (≥1)=reference]

[c]Dependent variable= Barthel scores at baseline and follow-up; independent variables include dummy variables of age, severity, comorbidity and frailty [categorized as 1 (robust), 2 (pre-frail), 3 (frail) =reference]; $^{*}p$ <.05, $^{**}p$ <.01