Circulating Blood Biomarkers In Older Adults With Frailty: The Irish Longitudinal Study on Ageing (TILDA

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Background & Aim

The concept of frailty captures differential vulnerability to adverse health outcomes. Frailty represents biological ageing as distinct from, but related to, chronological ageing. Several circulating blood biomarkers have been linked to phenotype frailty in cross-sectional studies and in longitudinal studies in women (Women's Health and Aging Study - WHAS) and the older old (Newcastle 85+ Study). In this study we examined the relationships between three frailty instruments and circulating biomarkers in older adults in Ireland.

Methods

Samples
Participant data from adults aged 50+ years (n=4,548; mean age: yrs, 54% female) who completed a health centre assessment during the first wave of TILDA.

Biomarkers
Preliminary raw biomarker measurements by frailty status and frailty instrument are presented in Figure 1. Transformed and standardised measures allowed comparability of associations with frailty across the different biomarkers on different scales. A one unit increase represented an increase of 1 SD from the mean (Table 1).

Frailty
This was assessed using Phenotype Frailty (PF), Frailty Index (FI) and FRAIL Scale (FS) instruments (Figure 2).

Statistical Analyses
Weighted prevalence of frailty for each measurement was calculated and the frailty status were calculated (Figure 2). Multinomial logistic regression computed relative risk ratios (RRR) and p-values measuring associations between frailty and each biomarker adjusted for age, sex, education, smoking status, BMI, and the number of medications and supplements taken regularly (Table 1).
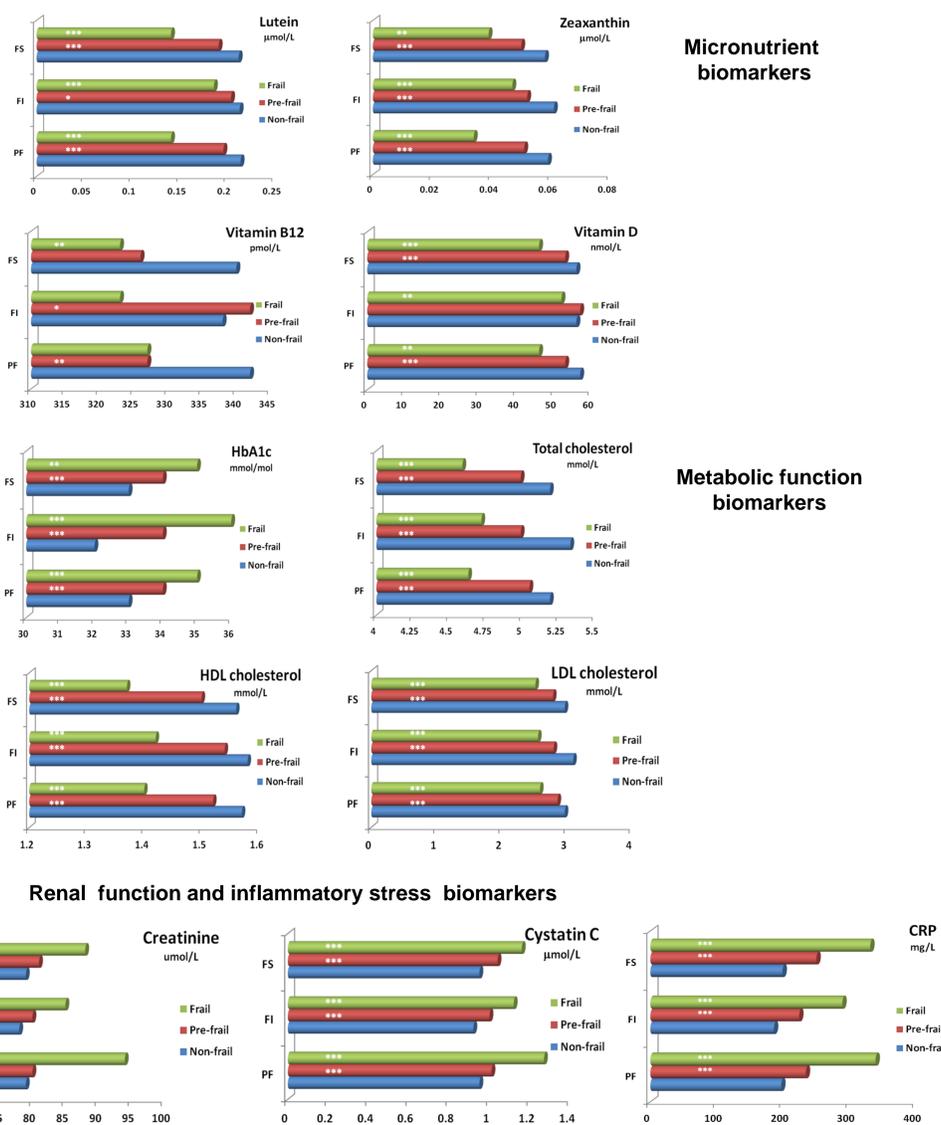

Figure 1. Micronutrient, metabolic function, renal function and inflammatory stress biomarkers (means) by frailty status and instrument. *p<0.05, **p<0.01,***p<0.001.
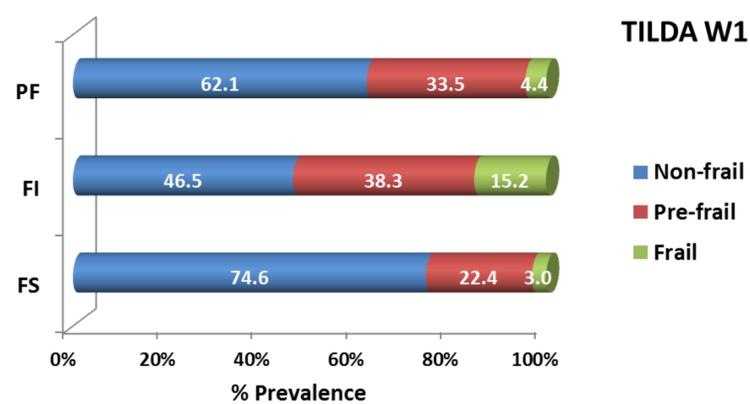

Figure 2. Weighted prevalence of frailty status, by frailty instrument.

Table 3. Adjusted associations between circulating biomarkers and frailty, by frailty instrument.

Biomarker (units)	Phenotype Frailty (PF)	Frailty Index Frailty (FI)	FRAIL Scale Frailty (FS)
	RRR (95% CI)	RRR (95% CI)	RRR (95% CI)
Lutein (mmol/L)	0.54*** (0.39 − 0.75)	0.86* (0.75 − 0.99)	0.55*** (0.43 − 0.71)
Zeaxanthin (mmol/L)	0.62*** (0.48 − 0.81)	0.90 (0.78 − 1.04)	0.65** (0.48 − 0.88)
Vitamin B12 (pmol/L)	0.86 (0.70 − 1.05)	0.96 (0.85 − 1.08)	0.87 (0.69 − 1.09)
Vitamin D (nmol/L)	0.82* (0.67 − 0.99)	0.91 (0.79 − 1.04)	0.87 (0.67 − 1.12)
C-reactive Protein (mg/L)	1.17 (0.93 − 1.48)	1.10 (0.95 − 1.26)	1.25 (0.93 − 1.68)
HbA1c (mmol/mol)	0.97 (0.82 − 1.13)	1.06 (0.94 − 1.20)	0.90 (0.75 − 1.08)
Total Cholesterol (mmol/L)	0.93 (0.77 − 1.13)	1.11 (0.98 − 1.27)	0.98 (0.78 − 1.22)
HDL Cholesterol (mmol/L)	0.87 (0.70 − 1.08)	0.87* (0.76 − 0.99)	0.82 (0.65 − 1.04)
LDL Cholesterol (mmol/L)	1.04 (0.86 − 1.26)	1.11 (0.98 − 1.26)	0.98 (0.79 − 1.22)
Creatinine (mmol/L)	1.10 (0.91 − 1.34)	1.02 (0.89 − 1.18)	1.16 (0.94 − 1.44)
Cystatin C (mg/L)	1.52*** (1.29 − 1.79)	1.16 * (1.00 − 1.34)	1.34** (1.09 − 1.65)

† Adjusted for age, sex, education, BMI and no. of medications and supplements taken regularly. *p<0.05, **p<0.01,***p<0.001.

Results

- Weighted prevalence of frailty and pre-frailty ranged between 3-15% and 22-38% respectively, across the frailty instruments.
- All biomarkers were significantly associated with frailty in unadjusted analyses, apart from vitamin B12.
- In adjusted analyses, Lutein and Cystatin c were negatively and positively associated with all three frailty measures, respectively.
- Zeaxanthin was negatively associated with Phenotype and FRAIL Scale frailty, in adjusted analyses.
- Higher vitamin D was negatively associated with Phenotype frailty only in adjusted analyses.
- HDL cholesterol levels were negatively associated with frailty as measured by the Frailty Index only.

Conclusions

Considerable variability exists in relation to associations between blood biomarkers and frailty, depending on the frailty instrument used. Given that no gold standard measurement of frailty has been agreed internationally, the identification of consistent cross-sectional associations with more than one frailty instrument strengthens the evidence that a biomarker may be correlated with frailty over time. However, causation cannot be inferred using cross-sectional data and this will be addressed using longitudinal data collected during waves 2 and 3 of the TILDA study.