

# Approximate Entropies of Resting State Continuous Neurocardiovascular Physiological Signals Are Associated with Physical Frailty in Older Adults <sup>†</sup>

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Frailty in older adults is characterised by dysregulation in multiple physiological systems. The frailty phenotype is defined on the basis of exhaustion, unexplained weight loss, weakness, slowness and low physical activity (one or two: pre-frail; 3 or more: frail). Our aim was to explore if increasing frailty is associated with the complexity of resting state physiological signals in a large cohort of community-dwelling older adults, enrolled as part of The Irish Longitudinal Study on Ageing (TILDA).

Systolic/diastolic blood pressure (SBP/DBP), mean arterial pressure (MAP), and heart rate (HR) were measured in 3154 participants (66.2% non-frail; 31.3% pre-frail; 2.5% frail) using a *Finometer*<sup>®</sup> device at 200 Hz; and frontal lobe oxygenation (tissue saturation index (TSI)) in 2749 individuals (66.3% non-frail; 31.3% pre-frail; 2.4% frail) at 50Hz using an *Artinis Portalite*<sup>®</sup> near infrared spectroscopy system. Data were acquired continuously during five minutes of supine rest and the last minute (downsampled to 5 Hz) was utilised in these analyses. The complexity of signals was quantified using approximate entropy (ApEn) with  $m = 2$  and an optimal  $r$  derived via multiple iterations, implemented in Matlab (*R2019a*). Statistical analysis was performed using multivariate linear regression models in STATA (*v14.1*), controlling for age, sex, education, antihypertensive medication, diabetes, number of cardiovascular conditions, smoking, alcohol, and depression.

Mean age for both groups was  $64.3 \pm 8.1$  years and 53% were female. The pre-frail group was associated with significantly increased ApEn for all measures investigated (sBP:  $\beta = 0.014$ ,  $p \leq 0.001$ ; dBP:  $\beta = 0.009$ ,  $p = 0.002$ ; MAP:  $\beta = 0.012$ ,  $p \leq 0.001$ ; HR:  $\beta = 0.011$ ,  $p = 0.003$ ; TSI:  $\beta = 0.009$ ,  $p = 0.002$ ). Likewise, the frail group was associated with further increased ApEn for all measures investigated (sBP:  $\beta = 0.031$ ,  $p = 0.002$ ; dBP:  $\beta = 0.028$ ,  $p = 0.003$ ; MAP:  $\beta = 0.038$ ,  $p \leq 0.001$ ; HR:  $\beta = 0.034$ ,  $p = 0.001$ ; TSI:  $\beta = 0.018$ ,  $p = 0.029$ ).

Approximate entropy seems to be a sensitive method to capture increasing signal complexity in multiple physiological systems associated with the frailty phenotype during resting state.



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