

# Orthostatic haemodynamics may be impaired in frailty<sup>†</sup>

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## Abstract

**Background:** orthostatic hypotension (OH) is a physical sign that reflects a final common pathway of various forms of disordered physiology, which is the hallmark of geriatric *frailty*. Fried *et al.* recognise three increasing frailty *phenotypes* in older people, based on measurements of *weight loss, exhaustion, grip strength, walking speed* and *physical activity*. Orthostatic haemodynamics have not been considered as markers of frailty in older people.

**Objective:** to classify a community sample of older people into three increasing frailty phenotypes and compare their orthostatic haemodynamics.

**Design:** cross-sectional study.

**Setting:** geriatric research clinic.

**Subjects:** a total of 442 subjects (mean age 72, 72% females) without dementia or risk factors for autonomic neuropathy.

**Methods:** the sample was classified according to modified Fried criteria. Orthostatic systolic blood pressure (SBP), diastolic blood pressure (DBP) and heart rate (HR) responses were monitored during an active stand with Finometer®.

**Results:** one hundred and ninety-eight subjects (44.8%) were classified as *non-frail*, 213 (48.2%) as *pre-frail*, and 31 (7.0%) as *frail*. Across groups, there was a significant increasing gradient in baseline HR ( $P = 0.008$ ) and decreasing gradients in Delta HR (i.e. maximum HR within 30 s—baseline HR) ( $P < 0.001$ ) and maximum HR by 30 s ( $P < 0.001$ ). On average, by 30 s after stand, non-frail subjects had recovered 98% of their baseline SBP, while pre-frail and frail subjects had recovered 95 and 92%, respectively ( $P$  for trend = 0.064).

**Conclusions:** the orthostatic HR response and, to a lesser extent, SBP recoverability, appear impaired in frailty. Orthostatic haemodynamics may be useful markers of frailty.

**Keywords:** *hypotension, orthostatic, haemodynamics, heart rate, frail, elderly, Finometer®*

## Introduction

Orthostatic hypotension (OH) is the most common disorder of blood pressure regulation after essential hypertension and in normal older subjects the prevalence is reported between 5 and 30%, increasing with age [1, 2]. The prevalence of OH depends on the population studied and the definition used in quantifying the degree of OH

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[3]. OH is associated with cardiovascular and cerebrovascular disease and with increased risk of falls, syncope and death [4, 5].

In comparison with the traditional measurement with sphygmomanometer or oscillometric blood pressure monitor, the assessment of orthostatic haemodynamic responses with continuous non-invasive measurement of finger arterial blood pressure has the advantage to offer a continuous pattern of response which can be visualised and analysed, not only for blood pressure but also for derived haemodynamic parameters.

OH has been defined as a sign that reflects 'a final common pathway of various forms of disordered physiology' [6],

which is the hallmark of *frailty*. Biologically, it is plausible that OH, reflecting disordered haemodynamic equilibrium, could be a manifestation of a wider process of multisystem dysregulation. In 1998, Masaki *et al.* suggested that ‘OH may be a marker for physical frailty’, in the light of their results that OH was a powerful predictor of mortality in the Honolulu Heart Program [7]. In 2007, Ejaz *et al.* argued that ‘it is perhaps not surprising that OH is more prevalent in frail individuals, because frailty is the cumulative effect of age, disease, disuse, and reduction in various physiologic reserves’ [8]. Despite suggestions that OH may be a sign of frailty, no studies to date had attempted to test this hypothesis.

While the operationalisation of frailty remains a challenging issue, Fried *et al.* recognise three increasing frailty categories or *phenotypes* in older people: *non-frail*, *pre-frail* and *frail* [9]. Their definition is based on measurements of *weight loss, exhaustion, handgrip strength, walking speed* and *physical activity*.

Our aim was to classify a sample of Irish community-dwelling older people into three increasing frailty groups and compare their orthostatic haemodynamics, looking for the presence of gradients.

## Methods

### Setting

Subjects were assessed at the Technology Research for Independent Living (TRIL) Clinic in St James’s Hospital (SJH), Dublin, between August 2007 and May 2009. The Clinic offers a multidisciplinary outpatient assessment to community-dwelling people aged  $\geq 60$  years. The majority of subjects (66.8%) were *self-referrals* for ‘health check’ attracted by our website ([www.trilcentre.org](http://www.trilcentre.org)) and/or articles in the local media; the rest (33.2%) were *referrals from health professionals* (e.g. SJH Emergency Department and local general practitioners) for further assessment of subjects with history of falls.

### Subjects

Of 624 community-dwelling subjects aged  $\geq 60$  years who registered as participants over the period, 608 had a continuous non-invasive measurement of finger arterial blood pressure. Active stand data could not be saved for 10 subjects, resulting in a sample of  $n = 598$  available for analyses.

### Exclusion criteria

All 598 active stands were reviewed and 11 excluded due to poor quality signals (i.e. artefacts, excessive signal fluctuation) and/or violation of the active stand protocol (e.g. *Physiocal* not switched off before stand leading to signal interruptions).

To minimise self-report bias, we excluded subjects with a Mini-Mental State Examination (MMSE) score of  $< 23$ , a cut-off that has been proved as optimal when screening for

dementia in an Irish community setting [10]. To avoid confounding by autonomic failure, we excluded subjects with Diabetes mellitus, Parkinson’s disease, severe chronic renal failure (defined as Cockcroft–Gault estimated glomerular filtration rate  $< 30$  mL/min), vitamin B12 or red cell folate deficiency. Subjects with cardiac pacemaker were also excluded.

The final sample was composed by 442 subjects, mean age 72.1 years (standard deviation (SD) 7.1); 317 (71.7%) were females.

### Active stand protocol

Subjects underwent a lying-to-standing orthostatic test (active stand) with non-invasive beat-to-beat blood pressure monitoring by the Finometer<sup>®</sup> Pro device (Finapres Medical Systems BV, Amsterdam, The Netherlands, [www.finapres.com](http://www.finapres.com)). For a description of the active stand protocol, please see the Supplementary data available in *Age and Ageing* online, Appendix S1. After standing, the blood pressure was monitored for 3 min; immediately after the test, subjects were asked to report whether they had felt *dizziness, faintness* or *light-headedness* (i.e. orthostatic intolerance, OI: yes or no).

### Active stand data processing

Active stand data were exported to Microsoft Excel<sup>®</sup> spreadsheets with the BeatScope<sup>®</sup> 1.1a software according to the 5-second averages method [11].

### Finometer<sup>®</sup> measures

For systolic blood pressure (SBP) and diastolic blood pressure (DBP), we computed the following measures:

- **Delta:** defined as the difference between *baseline* (average blood pressure between 60 and 30 s before stand) and *nadir* (lowest blood pressure point reached within 30 s following active stand).
- **Percentage of recovery:** maximum percentage of the baseline blood pressure recovered by 30 s, 1 and 2 min after stand.

For heart rate (HR), Delta was defined as the difference between the maximum HR achieved within 30 s after stand and the baseline. The HR at 120 s was also recorded as a percentage of the baseline HR.

### Frailty measures

We used the following five variables, selected among the ones in our protocol as the closest to criteria by Fried *et al.* [9]:

- **Exhaustion:** this criterion was present if the subject responded ‘yes’ to either (or both) of the following questions (based on the CES-D Depression Scale [12]): (i) ‘In the last week, did you feel in at least 3 days that everything

you did was an effort?'; (ii) 'In the last week, did you feel in at least 3 days that you could not get going?'

- Grip strength: it was measured three times in each hand with a dynamometer. The three measurements in each hand were averaged, and the higher of the two averages was selected (kg). We classified as frail by the *weakness* criterion those in the lowest 20th percentile of grip strength (stratifying by gender and quartiles of body mass index).
- Walking speed: it was measured with the GAITrite® walkway system (CIR Systems, Inc., <http://www.gaitrite.com>). Participants were asked to walk once along the walkway at their preferred walking speed, with no additional cognitive loading. The height-normalised gait velocity was recorded (i.e. absolute gait velocity divided by the average leg length [LL] of the subject, in LL/s). We classified as frail by the *slowness* criterion those within the lowest 20th percentile of normalised walking speed (stratifying by gender).
- Weight loss: this criterion was present if the subject reported at least 1 kg of unintentional weight loss in the last 3 months.
- Physical activity: this criterion was based on the number of hours per week spent walking outdoors. We classified as frail by the *low activity* criterion those in the lowest 20th percentile (stratifying by gender).

As per Fried *et al.*'s method, we defined as *frail* those with  $\geq 3$  of our criteria present; those with 1 or 2 criteria present were classified as *pre-frail*. The rest were classified as *non-frail*.

### Other characterisation variables

The frailty phenotypes were characterised according to the range of variables presented in Table 1.

The *consensus* definition of OH is a drop of at least 20 mmHg in SBP and/or 10 mmHg in DBP within the first 3 min of orthostasis [13].

*Initial* OH (IOH) is defined as a blood pressure drop, within 15 s after standing, of  $>40$  mmHg in SBP and/or  $>20$  mmHg in DBP, *with symptoms* of cerebral hypoperfusion (i.e. orthostatic intolerance) [14].

Subjects recalling at least 1 fall in the preceding 6 months were defined as fallers.

*Polypharmacy* was defined as the regular use of four or more medications.

The Charlson Comorbidity Index (CCI) was used as a marker of comorbidities [15]; it encompasses 19 medical conditions weighted 1–6 with total scores ranging from 0: lowest to 37: highest comorbidity. The CCI score was used unadjusted by age.

*Self-rated health* was assessed with a verbal rating scale from 0 (worst) to 10 (best).

For the definition of other characterisation variables, please see the Supplementary data available in *Age and Ageing* online, Appendix S2.

### Statistics

For the internal (i.e. construct) validation of our modified frailty definition, we used a structural equation model (AMOS 16.0), testing the fit of an underlying 'frailty' construct indicated by the five above-described frailty variables.

All other statistical analyses were performed with SPSS 16.0. Descriptives for dichotomous variables were given as percentages (%). Continuous variables were described as mean with SD, or median with inter-quartile range (IQR).

To test for linear trends (i.e. gradients) across frailty groups, we used the Chi-squared test for trend for dichotomous variables or Spearman's rank correlation coefficient for continuous variables.

Stepwise multiple linear regression analyses were performed to assess whether frailty was an independent predictor of selected haemodynamic variables in the face of other plausible predictors.

To adjust for multiple comparisons, the level of significance (alpha) was set at  $P < 0.01$  throughout. Statistical trend was defined as  $P < 0.05$ .

### Ethics

Local research ethics committee approval was obtained (SJH/AMNCH research ethics committee approval reference number 2007/06/13). All persons gave their informed consent prior to their inclusion in the study.

### Sources of funding

The TRIL Clinic is funded by Intel Corporation, the Industrial Development Agency (IDA) Ireland and GE Healthcare, with operational support from the Mercer's Institute for Successful Ageing at St James's Hospital Dublin ([www.misa.ie](http://www.misa.ie)). The financial sponsors played no role in the design, execution, analysis and interpretation of data or writing of the study.

### Results

The Figure in the Supplementary data available in *Age and Ageing* online, Appendix S3, shows the results of the validation of our modified frailty definition (in  $n = 442$ ). The RMSEA fit statistic was favourable (RMSEA = 0.033, 95% CI: 0.000–0.080,  $P = 0.665$ ).

Of the 442 subjects, 198 (44.8%) were classified as *non-frail*, 213 (48.2%) as *pre-frail* and 31 (7.0%) as *frail*. Table 1 shows their characteristics and Figure 1 shows their 5-second-averaged haemodynamic profiles.

### Haemodynamic responses

#### Systolic and diastolic blood pressure

On average, by 30 s post-stand, non-frail subjects had recovered 98% of their baseline SBP, while the pre-frail and frail had recovered 95 and 92%, respectively, representing a

Table I. Characterisation of the frailty groups

	Non-frail, n = 198	Pre-frail, n = 213	Frail, n = 31	P-value (linear trend)
<b>Systolic blood pressure (SBP)</b>				
Baseline SBP (mmHg)	158.3 (23.1)	162.3 (25.6)	160.1 (23.0)	0.155 <sup>a</sup>
Delta SBP (mmHg)	34.1 (17.3)	37.2 (18.8)	37.0 (23.8)	0.113 <sup>a</sup>
Max. SBP by 30 s (% baseline)	97.6 (11.2)	95.3 (12.8)	91.7 (17.7)	0.064 <sup>a</sup>
Max. SBP by 60 s (% baseline)	98.2 (10.8)	96.4 (12.4)	94.6 (16.7)	0.577 <sup>a</sup>
Max. SBP by 120 s (% baseline)	98.7 (11.6)	97.2 (13.9)	96.2 (19.0)	0.811 <sup>a</sup>
<b>Diastolic blood pressure (DBP)</b>				
Baseline DBP (mmHg)	78.4 (10.5)	78.9 (12.3)	76.6 (10.7)	0.859 <sup>a</sup>
Delta DBP (mmHg)	23.0 (11.4)	24.7 (12.0)	22.8 (14.0)	0.387 <sup>a</sup>
Max. DBP by 30 s (% baseline)	101.0 (12.1)	101.8 (15.2)	107.3 (13.2)	0.151 <sup>a</sup>
Max. DBP by 60 s (% baseline)	105.5 (12.4)	105.0 (14.4)	108.5 (13.6)	0.748 <sup>a</sup>
Max. DBP by 120 s (% baseline)	107.6 (12.6)	107.8 (15.3)	110.2 (13.8)	0.412 <sup>a</sup>
<b>Heart rate (HR)</b>				
Baseline HR (b.p.m.)	67.7 (10.7)	68.8 (10.6)	73.0 (9.2)	<b>0.008<sup>a</sup></b>
Delta HR (b.p.m.)	15.5 (6.2)	13.7 (10.5)	13.3 (7.1)	<b>&lt;0.001<sup>a</sup></b>
Max. HR by 30 s (% baseline)	123.7 (10.9)	120.6 (18.0)	118.8 (11.2)	<b>&lt;0.001<sup>a</sup></b>
HR by 120 s (% baseline)	110.1 (10.5)	109.0 (10.8)	111.8 (28.3)	0.675 <sup>a</sup>
<b>OH diagnoses</b>				
Consensus OH (%)	92.4	96.2	90.3	0.473 <sup>b</sup>
Initial OH (%)	12.7	22.6	38.7	<b>&lt;0.001<sup>b</sup></b>
<b>OI and falls</b>				
OI symptoms (%)	19.8	32.1	61.3	<b>&lt;0.001<sup>b</sup></b>
≥1 fall in the last 6 months (%)	6.6	16.0	35.5	<b>&lt;0.001<sup>b</sup></b>
<b>Demographics</b>				
Age (years)	70.5 (6.3)	72.9 (7.5)	76.6 (7.3)	<0.001 <sup>a</sup>
Female gender (%)	66.7	76.1	74.2	0.064 <sup>b</sup>
<b>Medications</b>				
Polypharmacy (%)	33.3	45.1	67.7	<b>&lt;0.001<sup>b</sup></b>
≥2 antihypertensives (%)	20.2	26.8	38.7	0.018 <sup>b</sup>
On beta-blocker (%)	15.7	21.1	32.3	0.024 <sup>b</sup>
On diuretic (%)	17.2	18.8	35.5	0.073 <sup>b</sup>
On ACE-I or ARA (%)	23.2	29.1	38.7	0.048 <sup>b</sup>
On calcium channel blocker (%)	9.1	9.4	16.1	0.396 <sup>b</sup>
On alpha-blocker (%)	2.0	4.2	3.2	0.311 <sup>b</sup>
≥2 psychotropics (%)	2.5	5.6	22.6	<b>&lt;0.001<sup>b</sup></b>
On antidepressant (%)	6.6	10.3	16.1	0.055 <sup>b</sup>
On benzodiazepine (%)	9.6	16.4	41.9	<b>&lt;0.001<sup>b</sup></b>
<b>Overall health</b>				
CCI: median (IQR)	1 (2)	1 (3)	3 (3)	<b>&lt;0.001<sup>a</sup></b>
Self-rated health	8.1 (1.3)	7.5 (1.6)	6.0 (2.4)	<b>&lt;0.001<sup>a</sup></b>
ADL score	23.1 (1.4)	22.6 (1.7)	22.0 (1.8)	<b>&lt;0.001<sup>a</sup></b>
IADL score	26.5 (0.9)	25.6 (2.1)	23.4 (2.9)	<b>&lt;0.001<sup>a</sup></b>
<b>Functional assessments</b>				
TUG (s)	8.0 (1.8)	10.0 (4.2)	15.8 (5.8)	<b>&lt;0.001<sup>a</sup></b>
BBS score	54.4 (2.3)	51.5 (5.6)	43.7 (9.5)	<b>&lt;0.001<sup>a</sup></b>
PEFR (L/min)	324.2 (126.8)	269.5 (100.8)	216.5 (91.8)	<b>&lt;0.001<sup>a</sup></b>
<b>Inflammatory markers</b>				
HbA1c (%)	5.6 (0.3)	5.7 (0.6)	5.8 (0.4)	0.080 <sup>a</sup>
Fibrinogen (g/L)	3.3 (0.6)	3.3 (0.6)	3.3 (0.7)	0.158 <sup>a</sup>
CRP (mg/L)	2.7 (2.7)	3.7 (5.2)	5.3 (6.3)	<b>0.001<sup>a</sup></b>
ESR (mm/h)	14.5 (10.3)	17.5 (14.0)	20.3 (11.4)	<b>0.006<sup>a</sup></b>
<b>Cognitive and psychological</b>				
MMSE score	28.2 (1.6)	27.6 (1.9)	26.2 (2.2)	<b>&lt;0.001<sup>a</sup></b>
MFES score	9.7 (0.8)	9.2 (1.2)	7.8 (1.9)	<b>&lt;0.001<sup>a</sup></b>
CESD-8 score	1.1 (1.5)	2.0 (1.9)	3.8 (2.5)	<b>&lt;0.001<sup>a</sup></b>
PSS score	7.8 (5.7)	10.4 (7.0)	11.6 (6.9)	<b>&lt;0.001<sup>a</sup></b>
<b>Frailty</b>				
Exhaustion criterion present (%)	0.0	31.0	71.0	<b>&lt;0.001<sup>b</sup></b>
Grip strength (kg): median (IQR)	25.5 (12.6)	18.6 (11.4)	14.2 (6.9)	<b>&lt;0.001<sup>a</sup></b>
Weakness criterion present (%)	0.0	31.5	51.6	<b>&lt;0.001<sup>b</sup></b>
Height-normalised gait speed (LL/s)	1.37 (0.21)	1.16 (0.31)	0.80 (0.32)	<b>&lt;0.001<sup>a</sup></b>
Slowness criterion present (%)	0.0	27.4	82.8	<b>&lt;0.001<sup>b</sup></b>

Continued

Table 1. Continued

	Non-frail, <i>n</i> = 198	Pre-frail, <i>n</i> = 213	Frail, <i>n</i> = 31	<i>P</i> -value (linear trend)
<i>Weight loss</i> criterion present (%)	0.0	24.9	48.4	<b>&lt;0.001<sup>b</sup></b>
Outdoor walking (hours/week)	5.2 (2.0)	3.3 (2.3)	1.3 (1.5)	<b>&lt;0.001<sup>a</sup></b>
<i>Low activity</i> criterion present (%)	0.0	25.4	71.0	<b>&lt;0.001<sup>b</sup></b>
No. frailty criteria: median (IQR)	0.0 (0.0)	1.4 (0.5)	3.2 (0.5)	<b>&lt;0.001<sup>a</sup></b>

<sup>a</sup>Spearman's rank correlation coefficient; <sup>b</sup>Chi-squared test for trend.

Quantitative variables are described as means and standard deviations (in brackets) unless otherwise specified. Significant *P* values (*P* < 0.01) are highlighted in bold and statistical trends (*P* < 0.05) are indicated in italics.

ACE-I, angiotensin-converting enzyme inhibitor; ADL, Activities of Daily Living; ARA, aldosterone receptor antagonist; BBS, Berg Balance Score; b.p.m., beats per minute; CCI, Charlson Comorbidity Index; CESD-8, Center for Epidemiological Studies Depression scale; CRP, C-reactive protein; DBP, diastolic blood pressure; ESR, erythrocyte sedimentation rate; HbA1c, glycosylated haemoglobin (%); HR, heart rate; IADL, Independent Activities of Daily Living; LL, leg length; MFES, Modified Falls Efficacy Scale; MMSE, Mini-Mental State Examination score; OH, orthostatic hypotension; OI, orthostatic intolerance; IQR, inter-quartile range; PEF, peak expiratory flow rate; PSS, Perceived Stress Scale; SBP, systolic blood pressure; TUG, time to get up and go.

close-to-trend gradient of SBP recoverability across frailty groups (*P* = 0.064). No statistical gradients in DBP were demonstrated.

### Heart rate

There was a statistically significant increasing gradient in baseline HR (*P* = 0.008), with frail subjects having, on average, 5 b.p.m. more than the non-frail group. There were significant decreasing gradients in Delta HR (*P* < 0.001) and maximum percentage of the baseline heart rate by 30 s (*P* < 0.001).

### Other gradients

As Table 1 shows, there were statistically significant gradients across frailty groups in the proportion of subjects with IOH (*P* < 0.001), OI (*P* < 0.001) and falls (*P* < 0.001); gradients were also seen in age (*P* < 0.001), polypharmacy (*P* < 0.001), psychotropic burden (*P* < 0.001), overall health (*P* < 0.001), functional assessments (*P* < 0.001), some inflammatory markers (C-reactive protein (CRP): *P* = 0.001; ESR: *P* = 0.006), cognitive and psychological tests (*P* < 0.001) and other frailty indicators (*P* < 0.001).

### Multivariable analyses

Table 2 shows the results of the stepwise multiple linear regression analyses. A set of 12 non-multicollinear predictors was tested against baseline HR, maximum % of baseline HR by 30 s and maximum % of baseline SBP by 30 s. The best independent predictors of baseline HR were beta-blocker (*P* < 0.001) and frail class (*P* = 0.004); for the maximum % of baseline HR by 30 s, the best predictors were age (*P* < 0.001), beta-blocker (*P* = 0.020) and diuretic (*P* = 0.046) and for the maximum % of baseline SBP by 30 s, they were CCI (*P* = 0.003) and MMSE (*P* = 0.012).

## Discussion

The aim of this study was to classify a sample of community-dwelling older people into three increasing frailty categories and compare their orthostatic

haemodynamic profiles. The baseline HR and early HR response and, to a lesser extent, the early SBP recoverability, appeared impaired in frailty on bivariate analyses.

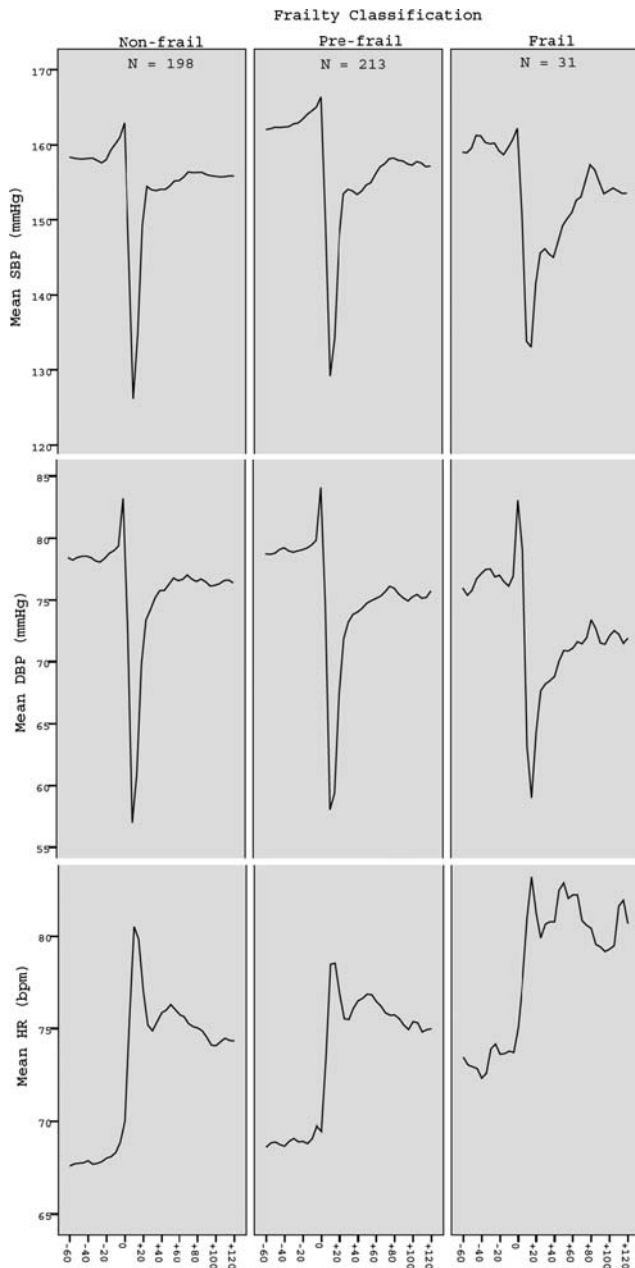
In multivariate analyses, frailty was (even in the face of beta blockers) an independent predictor of baseline HR, but in this sample, the early orthostatic HR and SBP responses were best predicted by *age* and *comorbidities*, respectively. Despite the fact that *ageing*, *comorbidities* and *frailty* are distinct clinical entities, there is growing evidence that they overlap and may be causally related [16].

The main haemodynamic finding of the study, namely the differences in baseline HR and orthostatic HR response across the frailty groups, are consistent with previous research. Regarding orthostatic HR responses, previous studies showed a tendency towards attenuation of the orthostatic HR response with *age* [17, 18].

Recently, the *Treating New Targets* trial showed that a resting HR  $\geq 70$  b.p.m. (NB: as in our frail subgroup) was associated with a 40% increased risk of all-cause mortality [19], in keeping with previous evidence that elevated resting HR is an independent risk factor for cardiovascular disease [20] and death [21]. Frailty is also a powerful predictor of mortality [22, 23] and, interestingly, Fried *et al.* recently suggested that HR dynamics might be useful for screening and monitoring of clinical vulnerability in older adults [24], and that cardiac autonomic control is indeed impaired in frailty [25].

A limitation of our study is that we could not use some of the original Fried frailty criteria [9]. However, our modified frailty definition had the expected associations with relevant *biological* and *psychosocial* parameters, in keeping with frailty being a holistic construct. In particular, and as previously reported [26], frailty had a strong association with *falls*.

Clinicians often implicate OH in the aetiology of falls in older people; however, concerns have been expressed that the clinical detection of OH is unlikely to be useful in predicting future risk of falling [27], and a systematic review found that OH does not predict falls after controlling for other factors [28]. Our work suggests that OH could be a marker of frailty; and since frailty is a better predictor of falls than OH, OH could be a useful indicator of the need



**Figure 1.** Haemodynamic profiles of the frailty groups (non-frail  $n = 198$ ; pre-frail  $n = 213$  and frail  $n = 31$ ). SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate.

for *multifaceted interventions* to target frailty (and, in turn, falls) [29]. In other words, *OH could be a screening tool for frailty* rather than an end diagnosis in itself.

Based on this pilot study, we postulate that a resting HR  $>70$  b.p.m. with an orthostatic HR increase of less than 20% above the baseline HR within 30 s after standing *may be*, even in the presence of beta-blockers, a marker of frailty in older people. In addition, reaching less than 92% of the baseline SBP within 30 s after stand may be a marker of comorbidities, including cognitive status [30]. Our study has various limitations, including the sample selection

**Table 2.** Results of the stepwise multiple linear regression analyses

Step no.	Variable	B	SE	$\beta$	T	P
Model 1: baseline HR (dependent variable)						
2	(Constant)	69.46	0.55		125.38	$<0.001$
	Beta blocker	-6.21	1.23	-0.23	-5.03	<b><math>&lt;0.001</math></b>
	Frail class	5.56	1.91	0.13	2.91	<b>0.004</b>
Model 2: maximum % of baseline HR by 30 s (dependent variable)						
3	(Constant)	147.10	7.07		20.82	$<0.001$
	Age	-0.35	0.10	-0.17	-3.55	<b><math>&lt;0.001</math></b>
	Beta-blocker	-4.19	1.79	-0.11	-2.33	<i>0.020</i>
	Diuretic	3.60	1.79	0.10	2.01	<i>0.046</i>
Model 3: maximum % of baseline SBP by 30 s (dependent variable)						
2	(Constant)	74.50	9.30		8.01	$<0.001$
	CCI	-1.01	0.34	-0.15	-3.01	<b>0.003</b>
	MMSE	0.83	0.33	0.12	2.54	<i>0.012</i>

Predictors entered in each model: age, gender, on beta-blocker, on diuretic, on angiotensin-converting enzyme inhibitor or aldosterone receptor antagonist, on calcium-channel blocker, on alpha-blocker, CCI, Independent Activities of Daily Living score, Time to get Up and Go, MMSE and frail class.

Significant  $P$ -values ( $P < 0.01$ ) are highlighted in bold, and statistical trends ( $P < 0.05$ ) are indicated in italics.

B, unstandardised regression coefficient; SE, standard error of B;  $\beta$ , standardised regression coefficient; HR, heart rate; SBP, systolic blood pressure; CCI, Charlson Comorbidity Index (unadjusted); MMSE, Mini-Mental State Examination score.

criteria and the lack of population representativity due to non-random sampling. In addition, the number of frail subjects ( $n = 31$ ) was small and underpower may have been an issue in some comparisons.

Further research in a larger population-based longitudinal setting such as the Irish Longitudinal Study of Ageing (TILDA, <http://www.tcd.ie/tilda>) will address many of the limitations of this preliminary study.

### Key points

- OH is seen in various forms of disordered physiology.
- A dimension of frailty is the dysregulation of multiple biological systems.
- We classified a sample of older people into three increasing frailty groups.
- The baseline HR and orthostatic HR response and, to a lesser extent, SBP recoverability appeared impaired in frailty.
- Orthostatic haemodynamics may be useful markers of frailty.

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## Conflicts of interest

None declared.

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## Supplementary data

Supplementary data mentioned in the text is available to subscribers in *Age and Ageing* online.

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## Agreement between equations estimating glomerular filtration rate in elderly nursing home residents and in hospitalised patients: implications for drug dosing

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### Abstract

**Background:** detecting chronic kidney disease (CKD) may have important implications for the management of older and frail people. We aimed at investigating whether clinical setting (nursing home: NH versus hospital: H) affects the agreement between glomerular filtration rate (GFR) values estimated by Chronic Kidney Disease-Epidemiology Collaboration (CKD-EPI), Cockcroft-Gault (CG) and Modification of Diet in Renal Disease (MDRD) equations.

**Design:** observational study.

**Setting:** comparison between NH residents and H patients.

**Subjects:** we used data from 177 NH residents, and 439 H patients.

**Methods:** the agreement between estimating equations and the odds of a discrepancy >25% between formulas in relation to setting (NH versus H) were investigated.

**Results:** the agreement between MDRD and CKD-EPI formulas was good either in NH ( $k = 0.82$ ) or H ( $k = 0.87$ ) patients, while corresponding figures for CG indicate only a fair agreement with CKD-EPI ( $k = 0.50$  for both populations). Setting (NH versus H) was associated with discordance between MDRD and CKD-EPI (OR = 3.97; 95% CI = 1.75–9.01), but not between CG and EPI (OR = 1.25; 95% CI = 0.87–1.81).