

Does vitamin D supplementation improve exercise capacity and quality of life in older heart failure patients?

A Randomised Controlled Trial

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Ageing and Health

Background

- Vitamin D insufficiency is common at high latitudes
- Vitamin D insufficiency is particularly common in older people
- Cardiovascular disease is responsible for 1/3 to 1/2 of decline in physical function in older people
- Observational evidence links low vitamin D levels to a range of cardiovascular diseases:
 - Ischaemic heart disease
 - Diabetes mellitus
 - Chronic heart failure
 - Hypertension
 - Stroke

Vitamin D in chronic heart failure

- Patients with CHF have a lot of symptoms, low exercise capacity and poor quality of life
- Part of this is due to skeletal myopathy
- Chronic inflammation is also part of the pathophysiology of CHF
- All CHF patients have deranged vascular function
- There are therefore multiple ways in which vitamin D might benefit CHF patients

■ Study question:

- Is vitamin D supplementation associated with an improvement in functional capacity and quality of life in older patients with vitamin D insufficiency and chronic heart failure?

Methods (1)

- Patients recruited from Dundee, Angus, Perth, Fife
- Medicine for the Elderly and cardiology clinics, heart failure clinics
- Wards (Medicine for the Elderly, General medicine)
- Community via advertising
- Via GP surgeries

■ Included if:

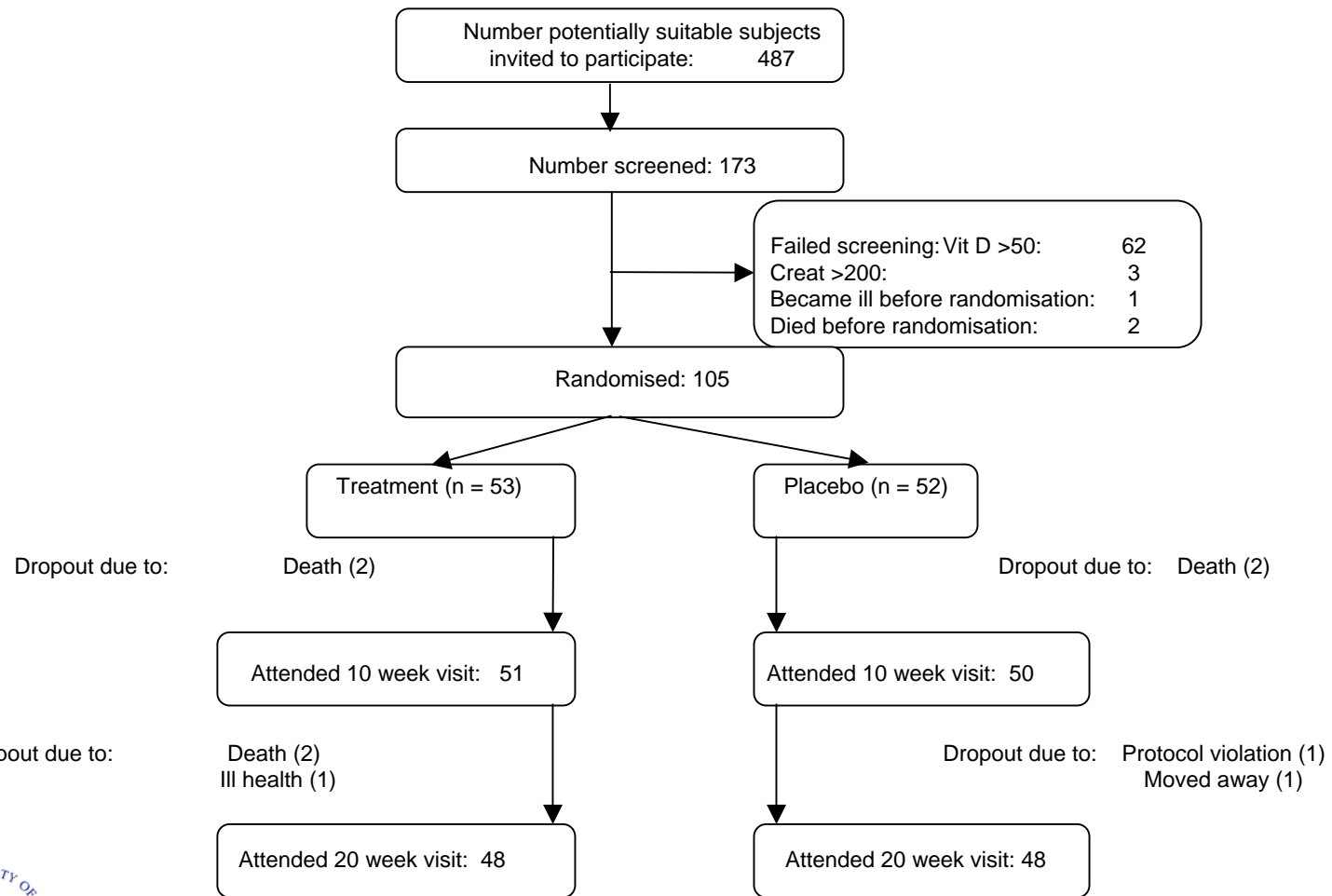
- Age >70 years
- 25OHD < 50 nmol/L
- Proven LV systolic dysfunction
- Clinical diagnosis of heart failure
- NYHA II or III

■ Excluded if:

- Creatinine >200 $\mu\text{mol/L}$
- LFT $>3x$ upper limit of normal
- Calcium >2.55 or <2.20 mmol/L
- Renal stones, sarcoidosis, metastatic cancer
- Unable to walk unaided
- Under investigation for recurrent falls

- Double blind, parallel group RCT
- Given 100,000 units oral vitamin D2 or placebo at baseline and 10 weeks
- Outcomes at baseline, 10 and 20 weeks
- Six min walk, timed up and go, daily activity, physical and psychosocial function, quality of life, BNP, TNF

Patient flow



Results (1) – baseline demographics

	Treatment (n=53)	Placebo (n=52)	<i>p</i>
Mean age (yrs) (SD)	78.8 (5.6)	80.6 (5.7)	0.10
Male sex	34/53	35/52 (67%)	0.73
NYHA II vs III	25 vs 28	22 vs 30	0.62
History of MI	25/53 (47%)	25/52 (48%)	0.93
On ACEi / ARB	41/53 (77%)	38/52 (73%)	0.61
On beta blocker	24/53 (45%)	30/52 (58%)	0.20
On spironolactone	14/53 (26%)	16/52 (29%)	0.62
Loop diuretic (frusemide equivalent dose per day) (mg) (SD)	37 (43)	52 (55)	0.10
Living alone	29/53 (55%)	26/52 (50%)	0.63
Walking aids	29/53 (55%)	21/52 (40%)	0.14
Baseline 25OHD (nmol/L) (SD)	20.5 (8.9)	23.7 (10.0)	0.10
Adjusted calcium (mmol/L) (SD)	2.35 (0.09)	2.35 (0.08)	0.64
Six min walk distance (m) (SD)	249 (116)	237 (108)	0.60
Timed up and go (s) (median, IQR)	15.0 (9.1)	15.5 (8.2)	0.51
Activity counts (median, IQR)	84636 (71442)	78403 (54517)	0.69
FLP (SD)	782 (175)	789 (165)	0.82
MLWHF score (SD)	23.6 (16.5)	24.7 (17.9)	0.76

Results (2) – Calcium and D

	Treatment	Placebo	Difference between groups (95% CI)	p
25OHD 0 v 10 wks (nmol/L)	22.9	2.3	20.6 (13.2 to 27.9)	<0.001
25OHD 0 v 20 wks (nmol/L)	19.5	1.3	18.3 (12.5 to 24.0)	<0.001
Calcium 0 v 10 wks (mmol/L)	0.04	0	0.04 (0.01 to 0.07)	0.01
Calcium 0 v 20 wks (mmol/L)	0.02	-0.02	0.04 (0.00 to 0.08)	0.03

Results (3) – Outcomes

	0 vs 10 weeks		0 vs 20 weeks	
	Treatment – placebo (95% CI)	p	Treatment – placebo (95% CI)	p
Six min walk (m)	-2.4 (-17.1 to 12.4)	0.75	-5.6 (-22.2 to 11.0)	0.51
Timed up and go (s)	0.21 (-1.79 to 1.37)	0.80	1.42 (-1.13 to 3.97)	0.27
FLP total	7.4 (-34.9 to 49.7)	0.73	18.9 (-26.2 to 64.0)	0.41
MLWHF total	3.8 (-1.1 to 8.8)	0.13	5.3 (0.5 to 10.2)	0.03
Activity counts	4241 (-8693 to 17174)	0.52	11003 (-3384 to 25389)	0.13
TNF alpha	0.14 (-0.38 to 0.67)	0.59	-0.05 (-0.58 to 0.48)	0.85
BNP	-99 (-208 to 10)	0.02*	-106 (-216 to 6)	0.08*

Results (4) – Safety

	Treatment	Placebo	p
Number developing hypercalcaemia (adjusted Ca >2.60 mmol/L)	2/51 (4%)	0/50 (0%)	0.25
Death	4/53 (8%)	2/52 (4%)	0.34
Exacerbation of CHF	1/50 (2%)	4/50 (8%)	0.18
Metabolic inc acute kidney injury	0/50 (0%)	3/50 (6%)	0.12
Number developing hypotension (SBP<90mmHg)	2/51 (4%)	2/50 (4%)	0.70
Falls / fractures	2/50 (4%)	5/50 (10%)	0.22
Patients with at least 1 adverse event	20/53 (38%)	25/52 (48%)	0.28
Hospitalisation	13/53 (25%)	11/52 (21%)	0.68

Conclusion

■ Vitamin D in CHF:

- Does not improve physical function
- May worsen quality of life – how?
- May improve daily activity – how?
- No serious safety problems seen but insufficient size to exclude safety problems
- No evidence of benefit in CHF from 2 trials now; not powered for death/hospitalisation
- Is a bigger dose needed?

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