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Original Scientific Paper

Vascular status and physical functioning: the association between vascular status and physical functioning in middle-aged and elderly men: a cross-sectional study

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Background **Living independently is an important component of quality of life. Cardiovascular diseases are prominent among the chronic conditions that predispose elderly people to functional limitations and disability, which impair quality of life. Insight into factors that play a role in the development process of limitations and disability of patients with subclinical cardiovascular diseases will aid in the development of preventive interventions. The aim of this study was to investigate the association of vascular status with muscle strength and physical functioning in middle aged and elderly men.**

Design **The study is a population-based cross-sectional study in 400 men aged 40–80 years, independently living at the time of enrolment, performed in the University Medical Center Utrecht in The Netherlands.**

Methods **Vascular status was measured noninvasively with ankle arm index, pulse wave velocity and intima–media thickness. Muscle strength was measured by isometric grip strength and physical performance was measured by Guralniks Physical Performance Score.**

Results **After adjustment for confounders, no associations were found between vascular status and physical functioning. Stratifying did not reveal subgroups, such as older age, in which an association was present.**

Conclusion **Contrary to former study results, this study showed no age-independent association between the extent of vascular damage and physical performance and muscle strength.** ***Eur J Cardiovasc Prev Rehabil*** **17:211–216 © 2010 The European Society of Cardiology**

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Introduction

Living independently is an important component of quality of life. Functional decline is one of the greatest threats for independence [1,2] because it can lead to functional limitations such as motor, cognitive and sensory limitations and eventually to limitations in (instrumental) activities of daily living, role and social functioning, so called disability [3–5]. At least half of end-stage disability results from progressive functional decline [3]. The other part is a result of acute clinical events [6]. The prevalence of disability in community-dwelling elderly is estimated at 20–30% [1].

Chronic disease, in particular cardiovascular disease (CVD) is an important determinant of functional decline in elderly persons [6,7]. A study in 1288 elderly persons showed that over 25% of disability was attributable to CVD [1].

Clinically manifest CVD is preceded by subclinical CVD, which reflects the extent of atherosclerosis and associated vascular damage. Noninvasive subclinical CVD measures, such as pulse wave velocity (PWV), carotid intima–media thickness (IMT) and ankle arm index (AAI) reflect different entities of the vascular status [8,9] and are shown to be significant predictors of incident CVD [9]. They have recently been used as main outcomes in clinical trials [10,11].

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Handgrip strength has been used as an indicator of overall muscle strength. It has been showed that middle-aged men with higher handgrip strength were protected from old age disabilities [5,12]. Lower extremity function can be measured with physical performance (PP) tests [13]. Across diverse populations decreasing performance seemed to be related to increasing risk of disability [4,13]. Performance measures can capture a hierarchy of functioning in persons who are not disabled and even in those who are well functioning [4].

It is well known that already in younger and middle-aged populations vascular damage exists [9,14,15] long before it is clinically manifest. However, it is less clear whether vascular damage when not yet symptomatic is already associated with decreases in muscle strength and PP.

If true then lower levels of subclinical CVD might predict not only better survival but also lower rates of functional decline [16]. Insight into future limitations and disability of patients with subclinical CVD will aid in the development of preventive interventions. The few studies that have been carried out to describe the association of vascular status with PP did indeed find decreased PP when the extent of atherosclerosis was higher [16–18]. However, these studies were performed in elderly people (age $\geq$ 65 years) and only one study focused on PP as main outcome.

The aim of this study was to investigate the association of vascular status with muscle strength and lower extremity function in middle aged and elderly men.

Methods

Study design and population

We conducted a cross-sectional study in 400 community-dwelling men aged 40–80 years, independently living at time of enrolment. Details of procedures have been published earlier [19]. The study was approved by the institutional Review Board of the University Medical Center Utrecht and written informed consent was obtained from all participants. Data collection took place between March 2001 and April 2002.

During two visits at the study centre, information was gathered about demographic and behavioural variables, cardiovascular assessment, handgrip strength, physical activity, cognition, Activities of Daily Living and prevalence of disease by physical tests and questionnaires.

Vascular assessment

Vascular status was measured noninvasively with AAI, PWV and IMT. AAI, PWV and IMT reflect different entities of vascular damage [8].

AAI, or the ratio of the ankle-to-brachial systolic blood pressure, reflects the presence of atherosclerotic vessel-wall abnormality of the arteries of the legs [20,21]. Blood pressure of arms and legs were measured in supine position by using a Doppler device (Huntleigh 500D; Huntleigh Technology, Bedfordshire, UK) and a random-zero sphygmomanometer. For each leg the higher of the two pressures was divided by the highest systolic pressure of both arms [20]. The lowest AAI in either leg was used in the analyses.

PWV is a validated method to quantify arterial stiffness and is associated with atherosclerosis [21]. PWV involves measurement of the transit time of the arterial pulse along the analyzed arterial segment and distance on the skin between both recording sites; the higher the PWV, the stiffer the arteries [22]. PWV was measured non-invasively using the SphygmoCor device (PWV Medical, Sydney, Australia) as described earlier [23]. The whole procedure was repeated three times per participant and the average PWV-value was used for the analysis.

Carotid IMT is a measure of the thickness of the intima and media layer of the carotid artery and is commonly used as a marker of atherosclerosis [23]. Ultrasonography of both the left and right carotid artery was performed using a 7.5-MHz linear array transducer (Ultramark IV; ATL, Bothell, Washington, USA) and IMT was calculated as described earlier [14]. The average of IMT of eight predefined angles was used in the analyses.

Physical functioning

PP or lower extremity function can be evaluated by using tests of gait speed, standing balance and ability to rise from a chair [4,13].

The three tests of standing balance were considered in hierarchical difficulty by assigning a single score of 0–4 for standing balance. For the 8-foot walk and repeated chair stands, those who could not complete the task were assigned a score of 0. Those completing the task were assigned scores of 1–4, corresponding to the quartiles of time needed to complete the task, with the fastest times scored as 4. A summary performance scale was created by summing the category scores for the walking, chair stand and balance tests, which ranged from 0 (worst performance) to 12 (best performance).

Isometric handgrip strength (IGS) has often been used as an indicator of overall muscle strength [5,12]. IGS was measured using an adjustable hand-held dynamometer (JAMAR dynamometer; Smith and Nephew, Memphis, Tennessee, USA) at the nondominant hand. The maximal value of three trials was noted.

Confounders/effect modifiers

A medical doctor obtained information on the prevalence of disease and the use of medication from a specified medical history. Diseases were classified by using the

International Classification of Diseases 10th revision code system. Participants were asked about the current use of medications; these reports were checked by examining labels of drugs brought to the clinic.

Height and weight were measured in standing position without shoes. Participants were asked about marital status and living situation. The level of education was recorded and categorized as university, high, middle and low.

The participant's customary alcohol intake was estimated from self-report and was categorized as no, light (0–2 drinks/day), moderate (2–4 drinks/day), or heavy (> 4 drinks/day) alcohol consumption. Smoking was estimated from self-report and categorized as current, former and never smokers.

The questionnaire on mobility in elderly developed and validated by Voorrips *et al.* [24] was used to assess physical activity. It includes three items of physical activities during the preceding year: household activities, sporting activities and other physically active leisure time activities. Overall scores, divided into low, moderate and high physical activity, were used.

Data analysis

Descriptive analyses included calculation of means and standard deviation for continuous variables and frequencies for categorical variables. In a small proportion (maximal 6%) PWV, PP and IMT measurements were missing because of technical problems with the equipment at the moment of measuring. Doing the analyses on a 'filled in' dataset would result in more precise estimates [25]. Missing data were imputed by using the means.

Multiple linear regression analysis was used to estimate the association between the continuous outcome variable IGS and the determinants (all continuous). PP Score was dichotomized into normal functioning (10–12) and some difficulties (0–9). Association with the determinants was examined with logistic regression analyses.

In the first model crude beta's/odds ratio's and their 95% confidence interval were calculated, in the second model was adjusted for age and in the third model was additionally adjusted for educational level, comorbidity, use of antihypertension medicine, smoking and use of alcohol.

In secondary analyses, we performed stratified analysis according to the four age decades and according to physical activity.

Data analyses were performed using SPSS statistical software (version 15.0) (SPSS Inc., Chicago, Illinois, USA) and R (version 2.6.1) (The R Foundation for Statistical Computing, Vienna, Austria).

Results

General characteristics of the participants are shown in Table 1. The median age was 60 years (range 40–80 years), 355 men (88.8%) were married or cohabited; 391 men (97.8%) were living independently. CVD was prevalent in 68 men (17%) and muscle-joint complaints in 95 men (24%). Other chronic illnesses such as diabetes, pulmonary disease, thyroid disease, malignancy, genital disease and stomach, bowel and liver disease occurred in less than 14% of the participants. In total 100 men (25%) had one chronic illness and 94 men (23.5%) had two or more chronic illnesses. Mean PWV was 9.41 m/s and mean IMT was 0.82 mm.

Almost all men (93%) scored in the highest two categories in PP and over 40% of the men scored in the highest category. Mean grip strength was 43.3 kg.

Table 1 Characteristics of participants ($N=400$)

	n (%)	Mean (SD)
Demographic characteristics and prevalence of disease		
Age (years)		60.2 (11.3)
Body mass index (kg/m)		26.3 (3.5)
Muscle-joint complaints	95 (23.8)	
Cardiovascular disease[a]	68 (17.0)	
Coronary heart disesae	52 (13.0)	
Cerebrovascular disease	12 (3.0)	
Peripheral arterial disease	14 (3.5)	
1 chronic illness	100 (25.0)	
>2 chronic illness	94 (23.5)	
Cardiovascular characteristics		
Pulse wave velocity (m/s)		9.41 (2.4)
Mean intima–media thickness (mm)		0.82 (0.2)
Physical performance and muscle strength		
Physical Performance Score		
10–12	164 (41.0)	
7–9	207 (51.8)	
4–6	29 (7.2)	
0–3	0 (0.0)	
Isometric grip strength (kg)		43.3 (8.6)
Possible confounders		
Education		
Low	66 (16.5)	
Middle	114 (28.5)	
High	141 (35.2)	
University	79 (19.8)	
Smoking		
Current	97 (24.3)	
Former	217 (54.3)	
Never	86 (21.4)	
Alcohol		
Heavy (>4 units/day)	48 (12.0)	
Moderate (2–4)	88 (22.0)	
Light (0–2)	196 (49.0)	
None	64 (16.0)	
Missing	4 (1.0)	
Physical activity		
Low	43 (10.8)	
Moderate	141 (35.2)	
High	216 (54.0)	
Hypertension medication		
Yes	333 (83.2)	
No	67 (16.8)	

SD, standard deviation. [a]Total number. One person can be diagnosed with more cardiovascular diseases.

Table 2 Association of ankle arm index, pulse wave velocity and intima–media thickness with isometric grip strength using linear regression (*N*=400)

	Model 1			Model 2			Model 3		
	β	95% CI	*P* value	*β*	95% CI	*P* value	*β*	95% CI	*P* value
Ankle arm index	6.34	0.41 (12.27)	0.04	2.01	−3.21 (7.22)	0.45	−0.10	−5.30 (5.10)	0.97
Pulse wave velocity	−1.22	−1.55 (−0.89)	0.00	−0.23	−0.61 (0.15)	0.23	−0.16	−0.54 (0.22)	0.41
Intima–media thickness	−16.90	−22.08 (−11.74)	0.00	1.40	−4.73 (7.53)	0.65	1.65	−4.37 (7.68)	0.59

Model 1, crude model; Model 2, adjusted for age; Model 3, adjusted for age, educational level, comorbidity, use of antihypertension medicine, smoking and use of alcohol. CI, confidence interval.

Table 3 Association of ankle arm index, pulse wave velocity and intima–media thickness with physical performance, using logistic regression (*N*=400)

	Model 1			Model 2			Model 3		
	Exponent (*β*)	95% CI	*P value*	Exponent (*β*)	95% CI	*P value*	Exponent (*β*)	95% CI	*P value*
Ankle arm index	0.18	0.04 (0.79)	0.03	0.38	0.07 (1.85)	0.24	0.62	0.11 (3.44)	0.59
Pulse wave velocity	1.33	1.20 (1.48)	0.00	1.07	0.95 (1.21)	0.30	1.02	0.90 (1.17)	0.73
Intima–media thickness	31.43	7.72 (137.12)	0.00	0.68	0.11 (4.33)	0.68	0.52	0.07 (3.79)	0.52

Model 1, crude model; Model 2, adjusted for age; Model 3, adjusted for age, educational level, comorbidity, use of antihypertension medicine, smoking and use of alcohol.

Tables 2 and 3 show the associations of vascular status with IGS and PP. Higher PWV and IMT and lower AAI are associated with lower IGS (crude beta's). When adjusted for age (model 2) and further adjustment for possible confounders (model 3), these associations are attenuated and not statistically significant anymore. Good PP was associated with higher PWV and IMT and lower AAI (Table 3, model 1). In model 2 and model 3 no associations can be seen.

Age-stratified analyses and analyses stratified for physical activity showed comparable results. No strata differences could be seen.

Discussion

This study showed no independent association between the extent of vascular damage and PP and muscle strength. Stratifying did not reveal subgroups, such as older age, in which an association was present.

Two studies that have been carried out however did find decreased PP when the extent of vascular damage was higher. These cross-sectional studies [17,18] did show associations between higher extent of subclinical CVD and, respectively, worse PP and an increased likelihood of frail health.

Both studies did have different study populations than this study. The most important difference is the mean age; both studies contain men and women of 65 years or older, with a mean age of 73.5 years, whereas in this study a younger population has been studied.

The educational level seems a bit higher in this study, although, because of differences in definitions, it is difficult to compare. A higher level of education could be explained by the younger age of our population. As a higher level of education is associated with a healthier lifestyle, this could have been an explanation for our different findings, but compared with the study of Elbaz *et al.* [17] more people in our study were smokers (24 vs. 6%) or former smokers (54 vs. 30%) and mean BMI was slightly higher in our study (26.3 vs. 25.6). In addition, mean IMT was lower (0.69 vs. 0.82) however, the fact that measurements were done on a different part of the common carotid artery hampers valid comparisons [17].

Newman *et al.* [18] did not provide information about lifestyle factors. They used 'frailty' as outcome, which includes more than just PP and muscle strength and therefore it is difficult to compare results. Maximum IMT was higher in this study than in ours, even though they calculated it only in the participants without clinical CVD history. This could explain a part of our different results, but too little information is given to make a good comparison between the study populations.

Several possible methodological limitations of the study should be mentioned. We were interested in the extent of vascular damage in all stages. Therefore, initially we also included participants with a history of CVD. As declined physical functioning can be a consequence of having CVD, we repeated the analyses excluding participants with a history of CVD. This did not change our findings. In addition muscle-joint complaints could affect physical functioning independent of vascular disease, however analysis restricted to participants without muscle-joint complaints did not change the results either.

Although with a cross-sectional design causal relations can never be shown, the aim of this study is aetiologic. Traditionally in aetiologic studies the relationship between two specific factors is explored. The past few years the idea is gaining territory that within the body processes never stand alone but always occur in combination and more or less interact with each other. Therefore analyses should take this into account [25]. In additional analyses, we combined PWV, IMT and AAI measurements to one variable for vascular status by differentiating participants with measurements in both the highest quartiles of PWV and IMT as well as the lowest quartile of AAI and other participants. There were no statistical differences in grip strength or PP between the two groups.

We assumed a linear association between the extent of vascular disease and functional decline. Several investigators argue that this association, if there is any, is certainly not linear. One longitudinal study for example showed a nonlinear association between the extent of subclinical vascular damage, measured by IMT, AAI and the likelihood of 'successful aging' [16]. Different populations, according to seriousness of the vascular damage had different strengths of associations. However, our data did not indicate nonlinearity. Several possible explanations can be thought of.

First only men in reasonably or good physical condition, who were capable of coming to the study centre independently, could participate in the study. Furthermore men with not too serious manifest CVD and/or muscle-joint complaints entered the study but men with advanced functional limitations did not. Although variation in vascular damage in this study is properly spread, it is possible that by excluding men with advanced functional limitations, men with extended vascular damage were also excluded. Functional limitations could have been the result of advanced CVD and corresponding vascular damage [26]. In contrast, underlying causes of functional limitations such as osteoporosis could have led to higher levels of circulating calcium and therefore higher vascular damage [27]. In both cases by excluding these participants more serious levels of vascular damage and therefore possible associations could have been missed.

Second in several studies and also in this study IMT is suggested to be an intermediate variable [16,17] between vascular risk factors and CVD. Newman *et al.* [16] however did find associations between the extent of vascular damage with 'successful ageing' independent of CVD. They suggest that arterial disease accelerates important age-related declines. By excluding participants who were not capable of reaching the study centre by themselves, it is also possible that these age-related declines, including decreased muscle strength and PP, were excluded and therefore no associations can be shown.

Conclusion

Crude associations between vascular damage and muscle strength and PP have been found, but contrary to former study results these associations were not age independent.

Izaks and Westendorp [28] define ageing as the accumulation of damage to somatic cells leading to cellular dysfunction and argue that 'normal' ageing does not exist and that various component causes together explain changes that occur with age. Following this theory an interesting question that needs to be answered in future research is which component causes in the variable 'age' are responsible for the attenuating of the crude association. Longitudinal data is needed to be able to say more about this question and possible causal relationships and associated explanations between vascular damage and physical functioning.

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