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Occupational class differences in ankle-brachial index and pulse wave velocity measurements to detect subclinical vascular disease

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Abstract

Background: *High pulse wave velocity (PWV) and low ankle brachial index (ABI) have been proposed as surrogate end-points for cardiovascular disease (CVD).* ***Objectives:*** *In a cross-sectional setting, we aimed at assessing the distributions of PWV and ABI among occupational classes (OC) in a population-based ever-employed salaried sample.* ***Methods:*** *We enrolled 1388 salaried CVD-free workers attending a CVD population-based survey, the RoCAV study, and classified them into four OC, based on current or last job title: manager/director (MD), non-manual (NMW), skilled-manual (SMW) and (UMW) unskilled-manual workers. We derived brachial-ankle PWV and ABI from four-limb blood pressures measurements, then carotid-femoral PWV (cfPWV) was estimated. We estimated the OC gradients in cfPWV and ABI using linear and logistic regression models.* ***Results:*** *Compared to MD (reference category), UMW had higher age- and BMI-adjusted cfPWV mean values both in men (0.63 m/s; 95%CI:0.11-1.16) and women (1.60 m/s; 0.43-2.77), only marginally reduced when adjusting for CVD risk factors. Decreased ABI mean values were also detected in lower OC. The overall detection rate of abnormal cfPWV (≥12 m/s) or ABI (≤0.9) values was 28%. Compared to MD, the prevalence of abnormal cfPWV or ABI was higher in NMW (OR=1.77; 95%CI:1.12-2.79), SMW (1.71; 1.05-2.78) and UMW (2.72; 1.65-4.50). Adjustment for CVD risk factors used in risk score equations did not change the results.* ***Discussion:*** *We found a higher prevalence of abnormal values of arterial stiffness measures in lower OC, and these differences were not explained by traditional CVD risk factors. These may be presumably determined by additional work- and environmental-related risk factors.*

Introduction

Cardiovascular diseases (CVD) have a multifactorial causes and a great social impact, representing the leading cause of mortality worldwide (1). Metabolic, clinical, behavioural, environmental as well as occupational risk factors contribute to CVD incidence and outcomes, and prevention measures targeting these factors are needed to reduce the CVD burden (2).

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Primary prevention of CVD events is largely carried out through the identification of subjects at high risk according to prediction equations (3-5) including major recognised risk factors. Accuracy and clinical performance of these equations are still under evaluation, in particular in people classified at intermediate and low risk. In this line, several biomarkers have been identified and tested for improvements in accuracy and net reclassification. Recently published results of the MESA Study (6) identified high-sensitivity CRP, CHD positive family history, Ankle-Brachial Index (ABI) and a Coronary Artery Calcium (CAC) index as independent predictors of incident CHD/CVD in intermediate risk individuals, but with major improvement in CVD risk prediction accuracy for CAC and minor effects of other biomarkers. Another paper emphasizes that a two- or multi-stage risk assessment approach may lower the costs and increase screening accuracy (7). In the MORGAM-BiomarCaRE Collaboration, other biomarkers showing improvements in risk accuracy have been identified in European cohorts, in particular cardiac troponins (8, 9) and lipoprotein(a) (10), but further investigations are needed before they can be included in currently used CVD risk equations.

A separate approach to improve risk prediction is based on the identification of high-risk subgroups in the populations to be targeted to more intense prevention activities. Results from the MORGAM Project population-based cohorts showed that stratification by educational classes produces a sensible improvement in the accuracy of cardiovascular risk prediction equations across European regions (11). In the same MORGAM-BiomarCaRE population-based cohorts, we identified people in the low educational strata to be at higher risk of CHD (12) and stroke (13) events. Similarly, exploring the association between CVD risk and occupational classes in MONICA-Brianza cohorts, we found in skilled and unskilled manual workers an increased CVD risk of 1.5-2.0 times, as compared to non-manual workers (14). In terms of prevention, an adjustment of the risk scores taking into consideration the higher incidence in low social classes has also been proposed (11,15).

However, these strategies still fail to consider the additional contribution of environmental and occupational-related CVD risk factors. In a recently published study (16), American researchers estimated that only 40% of the socio-economic gradient in myocardial infarction rates could be attributable to traditional CHD risk factors, while 60% was attributable to other factors associated to the lower socio-economic classes. Occupational and environmental exposures are recognized risk factors for CVD (17). Environmental work exposures include air pollution (18, 19), high levels of occupational physical activity as well as sedentarism at work (20), and noise (19, 21). Organizational and psychosocial risk factors include long working hours (22) and work strain (23, 24). Most of such exposures are prominently more frequent in low socio-economic classes and then the work environment may be an opportunity for collaborations in cardiovascular disease prevention (25).

Then, a meaningful attempt to improve prevention in lower social classes might be to adopt easy measurable, non-invasive and low-cost techniques to early detect subclinical CVDs and then to carry on targeted and more intensive prevention attempts to reduce the risk, starting at the work place (26).

High pulse wave velocity (PWV) and low ankle-brachial index (ABI) represent indirect indicators of arterial stiffness and vascular damage and have been proposed as risk markers for cardiovascular disease with a potential clinical utility in CVD risk assessment. Recent meta-analyses showed that an increase in PWV corresponds to an increased risk of cardiovascular events and all-cause mortality (27-29). Similarly, ABI, the most used test for the screening of peripheral artery disease and the diagnosis of lower extremity artery disease, is also a well-recognized risk predictor for cardiovascular disease (30-32).

The aims of the present study are to assess the distributions of PWV and ABI measures and the prevalence of their abnormal values among occupational classes (OC) in a population-based ever-employed sample of senior adults recruited in the RoCAV Study (Northern Italy), and to estimate the contribution of CVD risk factors in explaining the observed differences.

Methods

Study sample

Subjects were part of the Risk of Cardiovascular diseases and abdominal aortic Aneurysm in Varese (RoCAV), a population-based study (33). Participants were inhabitants of Varese City in Northern Italy, randomly selected from civil registry through randomisation stratified for sex and 5-year age classes (age range: men 50-75 years, women 60-75 years). A total of 3777 people were recruited between 2013 and 2016, with an overall participation rate of 63.8%. The study was approved by the Varese Hospital Ethical Committee (approval ID n. 66/2011) and all participants provided written informed consent.

Data collection

Socio-economic status and lifestyle information were collected through standardized questionnaires, while a complete occupational history and self-reported data, validated with clinical records, of diagnosis and treatments of cardiovascular diseases (coronary heart disease and ischemic stroke, peripheral artery disease, claudicatio intermittens), diabetes mellitus, hypertension and hypercholesterolemia were collected by trained interviewers (33). Based on extensive information on cigarette smoking habits, subjects were classified as current smokers vs non-smokers and ever or never smokers. In a quiet room, trained operators measured the blood pressure three times on the dominant arm with participants sitting down for at least 5 min and waiting 1 min between measurements; the study variable for systolic blood pressure is the mean of the first two measurements. Height and weight were measured in subjects without shoes and wearing only light indoor clothing. Body mass index (BMI) was calculated as weight (kg)/height(m)^2. Blood samples were collected after overnight fasting and serum total- and HDL-cholesterol, and blood glucose were measured using commercial reagents and automatic analysers. Diabetes mellitus was defined based on positive history or when blood glucose was above 126 mg/dl. All methods adhered to the standardised procedures and quality standards of the European Health Examination Survey (EHES) (http://www.ehes.info/manuals.htm#manual) and of the WHO MONICA Project (http://www.thl.fi/publications/monica/manual/index.htm). Based on these risk factors we calculated CVD risk scores according to ESC-recommend SCORE equation (34) as well as on the Italian CUORE Study equation (35).

For each subject we assessed the current occupational status (employed, unemployed, housewife, retired), the current and last job titles, coded according to the ISCO-88 Classification (https://www.ilo.org/public/english/bureau/stat/isco/isco88/index.htm) and if salaried or unsalaried (entrepreneurs, self-employed, free-lance, professionals with honoraria). For retired or unemployed subjects we used the last job title. The present analysis refers to salaried employees only. Based on first digit ISCO codes the following four occupational classes were defined and used in the analysis: manager/director (ISCO Code 1); non-manual workers (ISCO Codes 2-5); skilled manual workers (ISCO Codes 6-7); unskilled manual workers (ISCO Codes 8-9).

Trained physicians performed measurements of Ankle Brachial Index (ratio between average distal and proximal pressures) and brachial-ankle Pulse Wave Velocity (speed of sphygmic wave in m/s corrected for the height of the subject) (36) with patient in supine position after 5 minutes of rest, using an automated oscillometric measurement BOSO-ABI System (Bosch Sohn GmbH U. Co. KG, Jungingen, Germany). This System allows simultaneous arm-leg blood pressure measurements at the four limbs (two consecutive measurements) and provides carotid-femoral PWV (cfPWV) estimated using a validated algorithm [cfPWV = 0.833 x baPWV - 2.33] (37). For the analysis, we used the average of right ABI and left ABI measurements. In addition, we defined the presence of Peripheral Artery Disease (PAD) for ABI ≤0.90 in at least one leg. cfPWV was similarly dichotomised using as a cut-off point 12 m/s (2), indicating an abnormal cfPWV for values equal to or above the cut-off.

Statistical analysis

cfPWV and ABI were measured among participants recruited after December 2014 and they are available in 1821 out of the 3777 study participants. We observed no difference in the prevalence of manual workers in the subsample with available cfPWV/ABI data as compared to the overall study sample. We further excluded No.=47 subjects with missing data on occupational classes; No.=275 engaged in non-salaried activities (housewifes or professionals); and No.=111 with known cardiovascular diseases (coronary heart disease and ischemic stroke, peripheral artery disease, claudicatio intermittens), leaving an available sample size for the analysis of 1388 ever-employed salaried workers. The association between OC and cfPWV or ABI (continuous variables) was estimated through linear regression models and Chi-Square Likelihood Ratio test for heterogeneity of OC (manager/director was used as reference). Age, smoking, BMI, systolic blood pressure, total and HDL cholesterol, diabetes, anti-hypertensive and anti-hypercholesterolemic treatment were included in the model as potential confounders. At first, models were stratified by sex; then, as the associations between OC and the outcomes were similar across gender-groups, we also reported gender-pooled analyses, additionally adjusting for gender. Similarly, we used logistic regression models to estimate the association between occupational classes and abnormal cfPWV or PAD (yes/no outcome variables; cut-offs reported above), adjusting for the same confounders listed previously. All analyses were performed using the SAS system software (release 9.4 for Windows, SAS Institute Inc. Cary, NC, USA).

Results

Sample characteristics stratified by OC are summarised in Table 1a and Table 1b for men and women respectively. In comparison to men, women were less likely to be manager/director (4.1% vs 16.5%) or skilled manual workers (13.6% vs 26.5%), and more likely to be non-manual workers (61.6% vs 41.3%) or unskilled manual workers (20.7% vs 15.7%). Current and ever cigarette smoking habits differ between OC, both in men and women: current and ever smokers prevalence were higher in low OC, in particular in unskilled manual workers; while in women only current smoker showed the same pattern of men, instead ever smoker were higher, indicating that non-smoking campaigns had been more effective in higher OC. Higher mean values of BMI, blood glucose and prevalence of diabetes mellitus were found in unskilled manual workers, in women only. We found no differences across OC in lipid profile, systolic blood pressure values, prevalence of atrial fibrillation, anti-coagulant and anti-platelet medications nor in 10-year absolute CVD risk based on the ESC-SCORE and the CUORE equations, both in men and in women.

Table 2 showed the distribution of age-adjusted cfPWV and ABI means values among occupational classes. CfPWV mean values and prevalence of increased cfPWV were higher in unskilled manual workers, in comparison to the other OC, the difference being more pronounced in women. ABI means were lower in lower OC in women only, but with the same pattern was observed in both gender groups. In addition, since cfPWV and ABI means were consistently similar in women and men thorough OC, we reported the distributions in the two gender groups together, further adjusting for gender, which show the consistency of the pattern described above. To better grasp the pattern, Figure 1 and Figure 2 show the age- and BMI- adjusted (black squares) as well as the multifactor-adjusted differences (grey diamonds), separately for cfPWV and ABI measures, across the occupational classes, keeping manager/director as the reference category. As shown in Figure 1, only the difference in CfPWV between unskilled manual workers and the reference category resulted significantly higher in men (0.63 m/s; 95% CI:0.11, 1.16 m/s) and women (1.60 m/s; 95% CI:0.43, 2.77), and as a consequence in both gender groups (0.93 m/s, 95% CI:0.46, 1.39). The difference mast only partially reduce when adjusting for other CVD risk factors. Instead, as shown in Figure 2, ABI mean differences when compared to managers/directors, resulted progressively reducing for non-manual, skilled manual and unskilled manual workers, with clearer trends for men and both gender groups combined. Again CVD risk factors multiple adjustments did not substantially modify the results.

Table 3 reports the results obtained considering the presence of either abnormal values of cfPWV or PAD, adjusting for age, sex and BMI (Models 1) and further adjusting for other risk factors (Model 2). The prevalence odds ratio (OR) of abnormal

Table 1a. Baseline characteristics of enrolled workers by occupational classes, men. The RoCAV Study

Men (No.=925)	Manager/ director	Non-manual	Skilled manual	Unskilled manual	p-value*
No., %	153, 16.5%	382, 41.3%	245, 26.5%	145, 15.7%	-
Age (years)	64.2±7.3	63.5±7.0	63.8±6.9	63.3±7.2	0.67
Current-smokers	13%	17%	18%	25%	0.04
Ever-smokers	51%	52%	52%	66%	0.02
Total cholesterol (mg/dL)	207.0±3.1	204.4±2.0	208.2±2.4	205.0±3.2	0.63
HDL cholesterol (mg/dL)	53.8±1.1	54.2±0.7	54.4±0.9	53.3±1.1	0.89
Blood glucose (mg/dL)	102.3±2.1	101.3±1.4	100.3±1.7	103.7±2.2	0.65
Systolic blood pressure (mmHg)	136.2±1.3	137.4±0.9	137.0±1.6	138.1±1.4	0.79
Body Mass Index (kg/m^2)	26.7±0.3	26.9±0.2	27.3±0.2	27.0±0.3	0.51
Positive history of Diabetes	15%	12%	12%	19%	0.11
Positive history of Atrial Fibrillation	4%	3%	2%	4%	0.70
Current treatment for					
Hypertension	37%	44%	40%	45%	0.41
Hypercholesterolemia	20%	21%	21%	28%	0.33
Antiplatelet treatment	17%	15%	16%	18%	0.90
Anticoagulant treatment	3%	3%	2%	4%	0.73
SCORE 10-year CVD risk (%)	5.6	5.4	5.5	6.0	0.16
CUORE 10-year CHD risk (%)	14.1	14.0	14.4	16.0	0.06

Table 1b. Baseline characteristics of enrolled workers by occupational classes, women. The RoCAV Study

Women (No.=463)	Manager/director	Non-manual	Skilled manual	Unskilled manual	p-value*
No., %	19, 4.1%	285, 61.6%	63, 13.6%	96, 20.7%	-
Age (years)	67.7±4.3	68.9±4.2	70.0±3.8	69.1±4.3	0.14
Current-smokers	4%	13%	2%	12%	0.01
Ever-smokers	50%	35%	12%	32%	0.001
Total cholesterol (mg/dL)	211.6±8.8	220.4±2.3	228.0±4.9	217.6±3.9	0.27
HDL cholesterol (mg/dL)	71.7±3.8	68.8±1.0	66.4±2.1	64.8±1.7	0.13
Blood glucose (mg/dL)	89.9±4.7	95.1±1.2	91.4±2.6	101.0±2.1	0.01
Systolic blood pressure (mmHg)	134.3±4.0	140.0±1.0	139.0±2.2	139.8±1.8	0.56
Body mass index (Kg/m^2)	23.6±1.0	25.3±0.3	25.8±0.5	27.3±0.4	0.001
Positive history of Diabetes	5%	6%	3%	17%	0.003
Positive history of Atrial Fibrillation	0%	3%	3%	2%	0.71
Current treatment for					
Hypertension	50%	47%	39%	44%	0.68
Hypercholesterolemia	22%	35%	22%	30%	0.14
Antiplatelet treatment	17%	18%	17%	14%	0.90
Anticoagulant treatment	0%	4%	2%	3%	0.60
SCORE 10-year CVD risk (%)	4.1	5.2	4.7	5.2	0.30
CUORE 10-year CHD risk (%)	6.5	7.5	6.8	8.1	0.34

In the table: age-adjusted mean (proportion) for continuous and dichotomous variables respectively, estimated at the sample mean age. For continuous variables, the estimated mean is reported ± standard error. *Testing the null hypothesis of no association between occupational classes and each feature, from linear (logistic) regression model with age as covariate for continuous and dichotomous variables respectively. The p-value is relative to the F Test (with 3df) or to Chi-Square Test (with 3df) for continuous and dichotomous variables, respectively.

values were significantly higher in the three lower OCs compared to manager/director, with the highest OR value for unskilled manual workers, in both men and women, and the prevalence OR in the two gender groups combined was 2.72 (95%CI:1.65-4.50). Again, adjusting for traditional CVD risk factors (Model 2) only modestly reduced the OR to 2.63 (95%CI:1.55,4.45).

Table 2. cfPWV and ABI mean values and prevalence of abnormal cfPWV# and PAD° by occupational classes at baseline. The Ro-CAV Study.

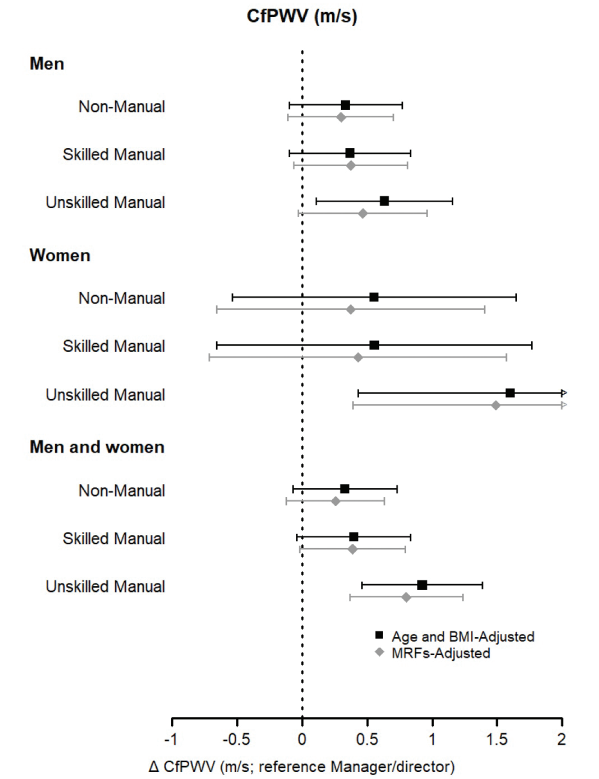
	Manager/ director	Non-manual	Skilled manual	Unskilled manual	*p**
Men					
No.	153	382	245	145	-
Mean cfPWV (m/s)	10.3±0.2	10.6±0.1	10.7±0.1	10.9±0.2	0.13
Mean ABI	1.167±0.009	1.144±0.006	1.139±0.007	1.147±0.009	0.10
Prevalence of abnormal cfPWV#	13%	22%	20%	26%	0.03
Prevalence of PAD°	2%	4%	6%	6%	0.17
Prevalence of abnormal cfPWV# or PAD°	15%	24%	23%	28%	0.05
Women					
No.	19	285	63	96	-
Mean cfPWV (m/s)	10.4±0.5	10.9±0.1	10.8±0.3	11.8±0.2	0.002
Mean ABI	1.137±0.022	1.106±0.006	1.068±0.012	1.086±0.001	0.01
Prevalence of abnormal cfPWV#	17%	26%	23%	43%	0.01
Prevalence of PAD°	0%	4%	6%	7%	0.41
Prevalence of abnormal cfPWV# or PAD°	17%	30%	27%	46%	0.01
Men and Women					
N	172	667	308	241	-
Mean cfPWV (m/s)	10.4±0.2	10.7±0.1	10.8±0.1	11.3±0.2	0.001
Mean ABI	1.153±0.009	1.132±0.004	1.118±0.006	1.125±0.007	0.01
Prevalence of abnormal cfPWV#	14%	23%	21%	32%	0.001
Prevalence of PAD°	2%	4%	6%	6%	0.06
Prevalence of abnormal cfPWV# or PAD°	16%	25%	25%	34%	0.001

In the table: age-adjusted mean (proportion) for continuous and dichotomous variables respectively, estimated at the sample mean age. Results for men and women combined are also adjusted for gender, and estimated at the observed prevalence of men in the sample. For continuous variables, the estimated mean is reported ± standard error. Mean ABI: average of Left and Right; #: Abnormal cfPWV: cfPWV≥12 m/s; ° PAD: either left or right side ABI ≤0.9; *Testing the null hypothesis of no association between occupational classes and each feature, from linear (logistic) regression model with age as covariate for continuous and dichotomous variables respectively. The p-value is relative to the F Test (with 3df) or to Chi-Square Test (with 3df) for continuous and dichotomous variables, respectively.

Discussion

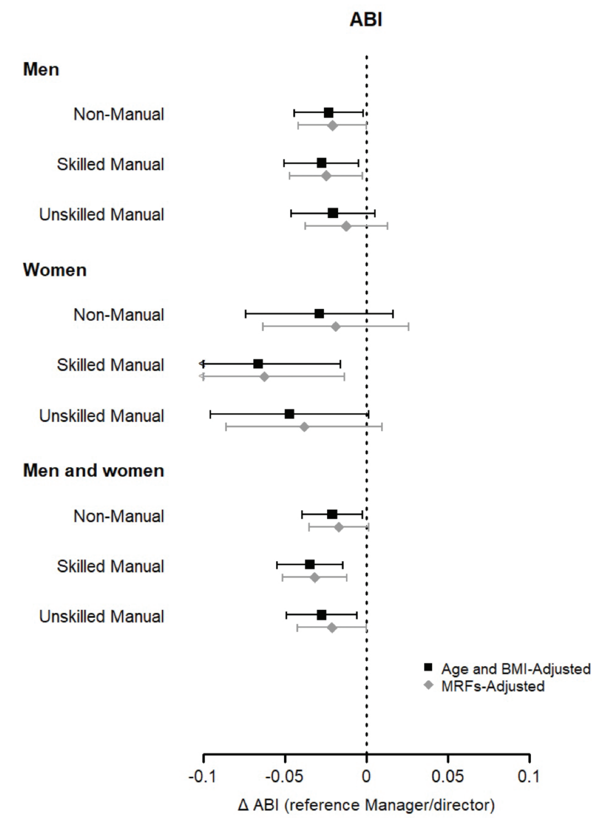
In our population-based sample of Italian ever-employed salaried workers, in both gender groups, cfPWV and ABI were found statistically significant different among occupational classes. Compared to manager/director, unskilled manual workers showed the worse values in all considered parameters, when considering cfPWV and ABI mean values as well as prevalence of abnormal values. Skilled manual workers showed higher ABI means and prevalence of abnormal values, and non-manual workers higher prevalence of abnormal values. Moreover, these differences were mostly independent of traditional CVD risk factors, including age, BMI, current cigarette smoking, total and HDL cholesterol, systolic blood pressure, diabetes, anti-hypertensive treatment, and lipid-lowering treatment.

The overall prevalence of abnormal cfPWV or PAD was 28%, indicating a relevant detection rate in clinical CVD-free subjects. CfPWV and ABI values are markers of arteriosclerosis and atherosclerosis respectively. According to European CVD Prevention Guidelines, cfPWV values above the threshold of 12 m/s are a conservative estimate of significant alterations of aortic function in middle-aged hypertensive patients (2). ABI values below 0.90 are considered a reliable marker of peripheral artery disease (38). Both of them have been pro-



MRFs-adjusted: age, BMI, current smoking, total and HDL-cholesterol, systolic blood pressure, diabetes, anti-hypertensive treatment, lipid-lowering treatment. Models for the gender-pooled analyses include also gender.

Figure 1. Mean differences of cfPWV (m/s) between occupational classes (reference: Manager/director), overall and by sex, adjusting for potential confounders.



Mean differences of ABI between occupational classes (reference: manager/director), overall and by sex, adjusting for potential confounders

Figure 2. Mean differences of ABI between occupational classes (reference: manager/director), overall and by sex, adjusting for potential confounders

posed as risk markers and surrogate end points for cardiovascular disease (29, 30).

Our findings then confirm previous studies (14) suggesting that lower occupational classes are at higher risk of CVD. Moreover, such excess risks cannot be fully explained by traditional CVD factors, indicating that other factors, including occupational, environmental and behavioural risk factors involved in determining arterial stiffness and CVD risk, can be of relevance in lower OCs. The MESA Study found an association between ABI and long working hours partially dependent on occupational classes (39) and independently of physical activity, suggesting the lack of time for consuming healthy meals on a regular basis and sleep deprivation as the main mediators of such an effect. Similar results were found in Taiwanese medical employees by Li-Ping Chou et al (40) examining the association between brachial-ankle PWV and various work-related conditions. In that study, brachial-ankle PWV was associated with medical profession and work type, as well as with long working hours, in addition to short sleep duration and all classical CVD risk factors; but not with job demand or control, social support and shift work (40). Caldwell et al. (41) showed that arterial stiffness in the lower limb increases after 2h of standing. Sedentarism at work is a recognised CVD risk factor, but also high levels of occupational physical activity is reported as an occupational risk factor for CVD (20). In addition, lower OC can be

Table 3. Association between occupational classes and presence of abnormal PWV[#] or PAD°, in men, women, and men and women combined, adjusting for potential confounders. The RoCAV Study

		Model 1				Model 2			
	No., n abnormal	OR	95%CI		*p*	OR	95%CI		*p*
Men					0.048				0.095
Manager/director	153, 27	REF	-	-		REF	-	-	
Non-manual	382, 96	1.73	1.06	2.83		1.79	1.07	3.01	
Skilled Manual	245, 61	1.67	0.99	2.82		1.75	1.01	3.03	
Unskilled Manual	145, 42	2.18	1.23	3.86		1.97	1.07	3.62	
Women					0.015				0.019
Manager/director	19, 3	REF	-	-		REF	-	-	
Non-manual	285, 90	2.20	0.60	8.10		2.00	0.52	7.73	
Skilled Manual	63, 20	1.90	0.47	7.64		1.76	0.42	7.47	
Unskilled Manual	96, 45	4.39	1.14	16.94		4.20	1.04	17.01	
Men and women					0.001				0.003
Manager/director	172, 30	REF	-	-		REF	-	-	
Non-manual	667, 186	1.77	1.12	2.79		1.75	1.09	2.82	
Skilled Manual	308, 81	1.71	1.05	2.78		1.76	1.06	2.92	
Unskilled Manual	241, 87	2.72	1.65	4.50		2.63	1.55	4.45	

OR = Odds Ratio estimated from logistic regression models. Model 1: Adjusted for age, BMI, and gender (gender-pooled analyses only). Model 2: Model 1 + current smoking, total and HDL-cholesterol, systolic blood pressure, diabetes, anti-hypertensive treatment, lipid-lowering treatment. ^Wald chi-square Test (3df); REF = Reference category; #: cfPWV≥12 m/s; °: either left or right side ABI ≤0.9

considered more exposed to air pollution, noise at work and at home.

According to current European Guidelines on CVD prevention (2), contributions from work settings are encouraged based on health promotion interventions aiming to promote healthy lifestyles. Evidences are accumulating that evoke a more comprehensive approach, the so called Total Worker Health, which implies to pay more attention in health promotion to sectors of the occupational forces which are at higher risk based on recognised occupational exposures, even for CVD prevention (25,42). Within this approach, detection of early measures of atherosclerosis may help in increasing the contribution of occupational physicians for CVD prevention. Benchimol et al. (43) showed advantaged in measuring ABI in workers seen for their annual routine examination by occupational physicians. Considering that arterial stiffness measures are not invasive and are easily determined, their adoption in work setting is relatively feasible. As reported by Park et al. (44), the addition of further measures, such as PWV, to the traditional CVD risk factors could improve the final cost-effectiveness of the collection of measures in CVD risk prediction. The results of the present analysis, which focuses on ever-employed individuals, suggest that individuals in lower OC should be the target of more intensive prevention activities not only at the work place, but even after retirement, when the subclinical conditions more frequently emerge, asking for an increased awareness and involvement of preventive cardiologists and general practitioners.

The main limitation of this study is its observational cross-sectional design. Further studies are needed on larger samples to assess if the early detection of subclinical atherosclerotic lesions may be effective to reduce to higher burden of CVD in lower OC. In addition, the advantage to include other non-invasive techniques, like carotid artery ultrasounds, should be carefully considered prospectively, as potentially useful tool to improve subclinical detections of CVDs in lower OC, once our findings have been generalized to different settings and populations. Finally, we used estimates of cfPWV calculated from measured values of brachial-ankle PWV

(37). Since brachial-ankle PWV reflects also characteristics of peripheral arteries (30), this should be taken into account when interpreting these results.

A strength of this study is a large set of data collected in a large population-based sample, using validated protocols and measurement methods, and computerised data collection tools to minimize missing data prevalence. Another strength is the satisfactory participation rate above 60%, consistent across age and gender groups (33),which helps to support generalizability of our findings, reducing the potential participation bias. The high overall prevalence of abnormal cfPWV or PAD identified (28%), indicates a relevant detection rates, supporting the effectiveness of the adopted screening procedures.

In conclusion, we found an association between cfPWV and ABI mean values, as well as prevalence of abnormal values, across occupational classes, independently on traditional CVD risk factors. Early detection of subclinical atherosclerosis in lower occupational classes allow grasping the contribution of additional work-, environmental- and behavioral-related factors to CVD risk. The clinical utility of such a prevention screening is supported by the high estimated detection rate in a primary prevention population. The feasibility of cfPWV and ABI measurement favors their use in CVD preventive screening at the workplace. Prevention efficacy should be confirmed in future prospective studies.

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