Ankle to brachial systolic pressure index at rest increases with age in asymptomatic physically active participants

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ABSTRACT

Background: It is commonly acknowledged that the ability to use the ankle–brachial index (ABI), a reliable way to diagnose atherosclerosis, decreases with age in the general population. The aim of this study was to determine the relationship between resting ABI and age in different populations.

Methods: 674 physically active participants with (active high risk, ACTHR) or without (active low risk, ACTLR) cardiovascular risk factors or/and sedentary (SED) subjects, aged 20–70 years. Systolic arterial pressure was recorded at rest and simultaneously with automatic sphygmomanometers at the arms and ankles. ABI was calculated as the ratio of the lowest, highest or mean ankle pressure to the highest arm pressure.

Results: Proportion of ABI_{min}<0.90 was 10.3% in SEDHR subjects versus 0.5% and 1.2%, respectively, in ACTHR and ACTLR groups. The averaged ABI value of each group was in the normal range in all groups (ABI>0.90) but was significantly lower in SEDHR compared with all active participants (p<0.001). Regression lines from ABI_{mean} versus age could lead to approximately +0.05 every 15 years of age in apparently healthy active participants (ACTLR).

Conclusion: ABI at rest increases with the increase in age in the groups of low-risk asymptomatic middle-aged trained adults. The previously reported decrease in ABI with age is found only in SEDHR subjects, and is very likely to rely on the increased prevalence of asymptomatic arterial disease in this group. The increase of ABI with age is consistent with the 'physiological' stiffness observed in ageing arteries even in the absence of 'pathological' atherosclerotic lesions.

Trial registration number: NCT01812343.

INTRODUCTION

Atherosclerosis is a widely prevalent disease, especially in Western countries. Numerous risk factors are known to increase the risk of atherosclerosis, including age, diabetes, hypertension, dyslipidaemia, smoking status and history of familial cardiovascular events. The decrease of ABI value with age could be due to the increased prevalence of asymptomatic peripheral artery disease in older participants.

Key messages

- This is the first study to report that resting ankle–brachial index (ABI) increases with age in asymptomatic and physically active participants without risk factors.
- The decrease of ABI value with age could be due to the increase in the prevalence of asymptomatic peripheral artery disease in older participants.
- This study suggests that the so-called borderline or low normal ABI (in the range 0.90–0.99) remains to be studied by considering the age of the participant.
asymptomatic participants. Indeed, during exercise, even very mild to moderate stenosis becomes symptomatic whereas these lesions remain asymptomatic in sedentary subjects. Hence, physically active and asymptomatic participants are very unlikely to present even mild stenosis. We hypothesised that: (1) on the one hand, in such physically active and asymptomatic participants without cardiovascular risk factors, instead of the usually reported negative relationship between resting ABI and age, we would find a positive relationship as a result of arterial wall remodelling with age, (2) on the other hand, using the same technique, the usual inverse relationship between ABI and age would be found in asymptomatic but sedentary subjects with cardiovascular risk factor, as a result of significant stenosis that remains asymptomatic due to low-activity level.

METHODS
This multicentre retrospective study was performed among patients with no history of cardiovascular disease and reporting no lower limb symptoms. All participants were referred to departments of sports medicine for the systematic evaluation of exercise performance or departments of vascular investigations to evaluate the presence or absence of PAD from ABI screening in patients with cardiovascular risk factors. In all participants, medical examination reports were used to bring out the presence or absence of cardiovascular risk factors (smoking status, hypertension, diabetes mellitus, dyslipidaemia, familial history of cardiovascular events). Although the gender of a participant could be considered a risk factor, each group consisted of males as well as females. Characteristics of the participants were recorded from a standard questionnaire, interview and physical evaluation. Only patients not reporting the use of cardiovascular drugs, lipid-lowering agent, any kind of limb pain at rest or exercise, or a history of cardiovascular disease, were included in the present study.

Procedure
Anthropometric data were recorded and ABI measured with automatic devices. Indeed, in the past few years, multiple devices have become available to automatically measure arm and ankle systolic pressures and determine ABI, in order to facilitate routine screening for PAD. These automatic devices are rapidly spreading and have been extensively used in previous studies. One of the major interests of automatic determination is to homogenise the measurement between various operators. Ankle and arm pressures were measured automatically using four Dynamap Critikon V100 15 cm large cuff sphygmomanometers (Johnson and Johnson, France), with the participant resting supine for at least 5 min. ABI was calculated for each leg using the highest arm pressure as a denominator. The numerator was either: the maximal (\(\text{ABI}_{\text{max}}\)), minimal (\(\text{ABI}_{\text{min}}\)), or mean (\(\text{ABI}_{\text{mean}}\)) of the two ankle pressures.

Subjects
From our database, we retrieved 674 participants fulfilling the inclusion criteria. Patients were divided into three groups. The first group (sedentary high risk, SED\(_{\text{HR}}\)), comprised of sedentary subjects referred to the vascular unit for systematic vascular investigations due to their risk factors. All these patients had one or multiple cardiovascular risk factors and reported no significant leisure physical activity. The other two groups consisted of asymptomatic physically active participants referred to sports medicine departments for the evaluation of their leisure physical activity. Among these asymptomatic and active participants, the second group included participants with one or more cardiovascular risk factors (active high risk, ACT\(_{\text{HR}}\)) and the third group included those reporting no cardiovascular risk factors (active low risk, ACT\(_{\text{LR}}\)). The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a priori approval by the institution’s human research committee. The study was registered in the NIH clinicaltrial.gov database under reference NCT01812343.

Statistical analysis
Analyses were performed using SPSS software, V.17. Quantitative variables are presented as mean±SD. Analysis of variance was used to compare continuous variables in the three groups. Linear regression was employed to describe the ABI-to-age relationship and its underlying hypotheses were verified. General linear model was used to compare the slopes of regression lines.

RESULTS
In brief, 674 participants aged 51.7±10.4 years; weight 76.7±14.6 kg; stature 1.72±0.08 m; body mass index (BMI) 26.0±4.8, were included in this study. Anthropometric characteristics and cardiovascular risk factors for each group are shown in tables 1 and 2.

SED\(_{\text{HR}}\) subjects logically had a mean weight and BMI significantly higher than active participants, either ACT\(_{\text{HR}}\) or ACT\(_{\text{LR}}\) (p<0.001). There were significant differences between the mean ages of the three groups (p<0.001).

Regarding cardiovascular risk factors (table 2), of interest to note is that in the ACT\(_{\text{HR}}\) subjects, the proportion of participants having one or two cardiovascular risk factors, was higher than for SED\(_{\text{HR}}\). However, SED\(_{\text{HR}}\) subjects were more likely to accumulate at least three cardiovascular risk factors. The major risk factor observed in ACT\(_{\text{HR}}\) subjects was smoking status and a history of familial cardiovascular events. In contrast, in SED\(_{\text{HR}}\) subjects, a large proportion of participants with diabetes was found.

Few participants had an \(\text{ABI}_{\text{LR}}\) <0.90. Taking the \(\text{ABI}_{\text{LR}}\) as a reference, proportion of \(\text{ABI}_{\text{LR}}\) <0.90 was 10.3%, 0.5% and 1.2%, in SED\(_{\text{HR}}\), ACT\(_{\text{HR}}\) and ACT\(_{\text{LR}}\) subjects.
respectively. Comparable results were observed using ABI_mean as reference—the proportion of ABI_mean<0.90 was 4.4%, 0.0% and 0.8%, in SEDHR, ACTHR and ACTLR subjects, respectively. Lastly, only six SEDHR subjects (2.4%) had an ABI_max<0.90. On average, as shown in table 1, the ABI observed in SEDHR subjects was lower than that in the other two groups, regardless of the method of calculation. In asymptomatic active participants, no significant differences were observed between the average ABI of high-risk or low-risk participants, regardless of the calculation mode (p=0.456, 0.931 and 0.663, respectively, for ABI_min, ABI_max and ABI_mean).

Finally, regression lines were ABI_mean=−0.02 age/10 +1.23 for SEDHR, ABI_mean=+0.01 age/10+1.14 for ACTHR and ABI_mean=+0.03 age/10+1.04 for ACHLR (figure 1). Slopes were significantly different between groups: p=0.01 for ACTLR versus ACTHR, p<0.001 for ACTLR versus SEDHR and p=0.04 for ACTHR versus SEDHR.

Comparative results were observed for relationships of ABI_min versus age and ABI_max versus age, as shown in figure 1.

**DISCUSSION**

To the best of our knowledge, this is the first study reporting resting ABI in asymptomatic and physically active participants without risk factors (ie, very unlikely to suffer even mild stenosis), in asymptomatic and physically active participants with risk factors, and in asymptomatic sedentary subjects with risk factors (ie, where mild to moderate PAD is likely to remain asymptomatic due to inactivity). Note that the average ABI value of this population was generally in the normal range (1.30>ABI_rest>0.90). The finding that ABI at rest does not decrease (but increases) with age in ACTLR is consistent with our initial hypothesis, and appears logical.

### Table 1

| Characteristics of included participants at rest | Active low risk (ACT_LR) | Active high risk (ACT_HR) | Sedentary high risk (SED_HR) |
|-------------------------------------------------|--------------------------|---------------------------|------------------------------|
| n                                               | 252                      | 218                       | 204                          |
| Males/females                                   | 223/29*                  | 175/43                    | 149/55                       |
| Age (years)                                     | 48.5±10.5†               | 50.4±9.5*                 | 56.9±9.1                     |
| Weight (kg)                                     | 74.1±11.4*               | 75.9±14.0*                | 80.9±17.8                    |
| Height (m)                                      | 1.74±0.07                | 1.73±0.09                 | 1.68±0.08                    |
| Body mass index (kg/m²)                         | 24.4±3.2*                | 25.2±3.8*                 | 28.7±6.1                     |
| Power output (W)                                | 249±55                   | 221±59                    | Not available                |
| Minimal ankle–brachial index (ABI_min)          | 1.15±0.10*               | 1.14±0.10*                | 1.08±0.14                    |
| Maximal ankle–brachial index (ABI_max)          | 1.20±0.10*               | 1.20±0.09*                | 1.16±0.14                    |
| Mean ankle–brachial index (ABI_mean)            | 1.17±0.09*               | 1.17±0.09*                | 1.12±0.13                    |

Data are presented as mean±SD.

*p Value <0.05, significantly different from SED_HR.
†p Value <0.05, significantly different from ACT_HR. p Value is a tendency of overall comparison.

### Table 2

| Occurrence frequencies of various risk factors of overall participants | Active low risk (ACT_LR) | Active high risk (ACT_HR) | Sedentary high risk (SED_HR) |
|---------------------------------------------------------------------|--------------------------|---------------------------|------------------------------|
| Number of risk factors (%)                                          | 100                      | 0                         | 0                            |
| 1                                                                   | 0                        | 78.9                      | 69.6                         |
| 2                                                                   | 0                        | 18.8                      | 16.2                         |
| 3                                                                   | 0                        | 2.3                       | 12.2                         |
| 4                                                                   | 0                        | 0                         | 2.0                          |
| Smoking status, smoker (active+former)/no smoker, n (%)             | 0/252                    | 183/35                    | 24/180                       |
| Smoker (active+former)/no smoker, n (%)                             | (0)/100                  | (83.9)/16.1               | (11.8)/88.2                  |
| Hypertension, n (%)                                                 | 0 (0)                    | 19 (8.7)                  | 62 (30.4)                    |
| Diabetes mellitus, n (%)                                           | 0 (0)                    | 2 (0.9)                   | 157 (77.0)                   |
| Dyslipidaemia, n (%)                                                | 0 (0)                    | 41 (18.8%)                | 47 (23.0)                    |
| Familial history of cardiovascular (CV) events, n (%)              | 0 (0)                    | 66 (30.3)                 | 9 (4.4)                      |
| Average of CV risk factors, n (%)                                   | 0                        | 1.2                       | 1.5                          |

Congnard F, et al. BMJ Open Sport Exerc Med 2015;1:e000081. doi:10.1136/bmjsem-2015-000081

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with the expected ‘physiological’ ageing of the arterial wall. On the contrary, we found the expected decrease of ABI with age in the SEDHR population. Interestingly, the slope of the relationship of ABI to age in the ACTHR subjects is half way between the two other regression analyses. We contend that these observations objectively support the assumption that the decrease of ABI value with age is due to the increase in the prevalence of asymptomatic PAD in older participants, whereas ABI ‘physiologically’ increases with age.

It is commonly accepted that ABI<0.90 at rest is the most common and agreed on value, having reported acceptable levels of sensitivity and specificity to detect PAD. Nevertheless, this cut-off was determined on populations with proven PAD or in advanced age populations. The results of our study present a ‘physiological’ trend of resting ABI to increase by approximately +0.05 every 15 years of age in apparently healthy subjects. Thus, the use of a cut-off point of ABI<0.90, could overestimate the prevalence of PAD in the young, while this could underestimate the prevalence of PAD in the elderly. This could also be an explanation for the fact that the sensitivity of ABI is reportedly decreased in elderly patients.

There are limitations to the present study. First, it may be that our observation results from a technical issue. Whether automatic devices are equally accurate in young or old participants has never been studied. The fact that automatically determined pressures overestimate the pressure that would be observed in manual recordings, especially for low-pressure values, cannot consistently be excluded. This potential overestimation should explain the difference between groups. Second, it could be argued that physically active patients are more likely to have higher ABI values than participants with low physical activity levels. This is also true, and we found a similar trend in our group in terms of average ABI value within each group. Nevertheless, the ABI to age relationship was analysed in groups with a relatively homogeneous activity level (Power Output ACTLR vs ACTHR: p=0.433). Third, we provide no argument that the increased trend of ABI with ageing in ACTLR is related to arterial stiffening. Previous studies have reported a weak but significant association between a high ABI and high pulse wave velocity. Further investigations are needed in ACTLR subjects to correlate ABI measurements to measurements of arterial stiffness. Fourth, no ultrasound imaging was carried out to exclude those patients who might have had mild to moderate arterial ultrasound lesions. We advocate that this would have been of little interest because, in sports-related claudication, even extremely localised and mild lesions may become symptomatic, as illustrated by endo-fibrosis in athletes. The sensitivity of ultrasound to detect these extremely moderate lesions would be relatively low. Inversely, we think that it is unlikely that the absence of decrease of ABI resulted from undetected severe stenoses, since ABI decreases with the severity of endoluminal lesions. Lastly, on the one hand, our groups show a very high proportion of males and
Caucasian participants. Thereby, our results would require confirmation due to the differences in ABI that are reported between males and females or between black and Caucasian participants.\textsuperscript{29} On the other hand, extrapolation to other automatic devices is needed as well as confirmation with manual recordings. It should be kept in mind that the variability of manual recording is high and depends on the observer experience. Using automatic devices allowed us to get rid of interindividual variability\textsuperscript{29} and to reduce the time of measurement.\textsuperscript{30}

In conclusion, the present study provides, for the first time, objective evidence that the ‘physiological’ change in ABI increases with age. This reinforces the belief that the decrease in ABI at rest with age observed in general population studies likely results from the increased prevalence of participants with subclinical PAD. This may also question whether the same resting ABI value should be used as a cut-off point in the youngest and oldest participants. Specifically, the present study suggests that the so-called borderline or low normal ABI (in the range of 0.90–0.99) is more likely to predict the presence of PAD in older than in younger patients.

Acknowledgements The authors would like to thank the CRC d’Angers, I Laporte and M Gernigon, for technical help.

Funding The study was promoted by the University Hospital in Angers and supported by grants from PHRC-IR 2012, SORMES, CDOS49, DDS49, Mairie d’Angers. FC benefits from the support of APOSS (IFEPSA).

Competing interests None declared.

Ethic approval This study and templates informed consent forms had been reviewed and approved by the Ethics Committee CPP-OUEST II (France).

Provenance and peer review Not commissioned; internally peer reviewed.

Data sharing statement No additional data are available.

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