Utility of estimated pulse wave velocity for assessing vascular stiffness: comparison of methods

Stefan Möstl¹*, Fabian Hoffmann¹.²*, Jan-Niklas Hönemann¹.², Jose Ramon Alvero-Cruz³, Jörn Rittweger⁴, Jens Tank¹ and Jens Jordan⁵.⁶

1 Department of Cardiovascular Aerospace Medicine, Institute of Aerospace Medicine, German Aerospace Center, Cologne, Germany
2 Department of Cardiology, University Hospital Cologne, Germany
3 Department of Human Physiology and Physical Sports Education, Faculty of Medicine, University of Málaga, Spain
4 Department of Muscle and Bone Metabolism, Institute of Aerospace Medicine, German Aerospace Center, Cologne, Germany
5 Institute of Aerospace Medicine, German Aerospace Center, Cologne, Germany
6 Chair of Aerospace Medicine, University of Cologne, Cologne, Germany

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*authors contributed equally

Corresponding author:
Jens Jordan M.D.
Institute of Aerospace Medicine
German Aerospace Center
Linder Hoehe
51147 Cologne, Germany
jens.jordan@dlr.de
Abstract

Background. Pulse wave velocity independently predicts cardiovascular risk. Easy to use single cuff oscillometric methods are utilized in clinical practice to estimate pulse wave velocity. We applied the approach in master athletes to assess possible beneficial effects of lifelong exercise on vascular health. Furthermore, we compared single cuff measurements with a two-cuff method in another cohort.

Methods. We obtained single cuff upper arm oscillometric measurements thrice in 129 master athletes aged 35 to 86 years and estimated pulse wave velocity using the ArcSolver algorithm. We applied the same method in 24 healthy persons aged 24 to 55 years participating in a head down tilt bedrest study. In the latter group, we also obtained direct pulse wave velocity measurements using a thigh cuff.

Results. Estimated pulse velocity very highly correlated with age ($R^2 = 0.90$) in master athletes. Estimated pulse wave velocity values were located on the same regression line like values obtained in participants of the head down tilt bedrest study. The modest correlation between estimated and measured PWV ($r^2 = 0.40$; $p<0.05$) was attenuated after adjusting for age; the mean difference between pulse wave velocity measurements was 1 m/s.

Conclusion. Estimated pulse wave velocity mainly reflects the entered age rather than true vascular properties and, therefore, failed detecting beneficial effects of lifelong exercise.

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Introduction

Aortic pulse wave velocity (PWV) which relates to vascular stiffness, independently predicts cardiovascular risk including stroke \(^1,2\). PWV values above 10 m/s have been suggested as threshold indicating increased risk \(^3\) and are included in current hypertension guidelines for assessing hypertension-mediated organ damage and guiding secondary prophylaxis \(^4\). Local PWV measurements are also feasible using two points close or more distant to each other as well as measurements of pressure-velocity loops at one single spot. However, the guidelines do not specify certain methods to measure PWV. Measurements at different sites including the thigh were used in large scale studies. However, this PWV-assessment is difficult to implement in busy clinics or during daily routine. Oscillometric blood pressure monitors estimating PWV based on age and blood pressure could simplify vascular assessment \(^1,5\). Indeed, estimated PWV correlates with age \(^6\) and invasively measured PWV \(^1\). These monitors operate observer-independent, are easy to use, and are, therefore, applied in clinical practice and in clinical studies alike \(^7\). However, in a study investigating beneficial effects of competitive life-long physical exercise in elite Masters Athletes, we obtained estimated PWV results suggesting that the approach adds little information to classical cardiovascular risk assessment. We decided comparing the methodology with aortic PWV measurements in an independent set of healthy persons participating in a head-down-tilt bedrest study.

Methods
During the 23rd Masters Athletics Championships 2018 in Málaga, Spain, we approached 163 master athletes. We excluded athletes with atrial fibrillation or significant cardiovascular disease assessed by echocardiography. In the remaining 129 athletes (88 men/41 women, 56±11 (range 35-86) years, 24.0±3.5 kg/m²), we acquired blood pressure, heart rate, and estimated PWV thrice on the same arm after 10 minutes supine rest (Arc-Solver-Algorithm, CardioCube, AIT, Vienna, Austria).

In 24 healthy participants (16 men/8 women, 33±9 years, 24.3±2.1 kg/m²) of the AGBRESA (artificial gravity bedrest) study, which was conducted in collaboration with NASA and ESA in Cologne, Germany, we assessed estimated PWV before head-down-tilt bedrest as described above. As the estimated PWV has been validated against invasive catheter measurements derived from the ascending aorta to the aortic bifurcation, we mimicked this approach non-invasively by measuring pulse wave arrival time from the electrocardiographic R-Peak to the arrival of the pulse wave at an oscillometric thigh-cuff. We corrected pulse wave arrival time for isovolumetric contraction time, the time from the R-peak in the ECG to aortic valve opening assessed by 2D-Pulsed-Wave-Doppler echocardiography. Corrected pulse wave arrival time represents pulse wave travel time from the aortic valve opening to the arrival at the thigh. Moreover, in contrast to the carotid-femoral PWV, this approach includes the ascending aorta and the aortic arc, which are commonly affected by aging-associated vascular disease. Dividing jugulum-thigh cuff distance by corrected pulse wave arrival time resulted in measured PWV.

All subjects provided informed consent and consent to publish before enrollment. The bedrest study as well as the study in master athletes were approved by the Northrhine-Medical-Association (Ärztekammer Nordrhein, 2018143 and 2018171) ethics committee and registered at the German Clinical Trial Register (DRKS00015677 and DRKS00015172).
According to Kolmogorov-Smirnov-Test, all data were normally distributed and results are reported as mean values ± standard deviation. Based on other cardiovascular risk-estimate-models, we used a quadratic regression model.

Results

Resting heart rate was 61±11 bpm and blood pressure was 128±15/78±8 mmHg in master athletes. Estimated PWV ranged from 5.5-14.5 with a mean of 8.3±1.8 m/s. In a quadratic regression model, age and mean arterial pressure predicted estimated PWV (beta-value 0.93 and 0.14, p<0.001), whereas sex and BMI had no influence. The model explained 95% (R²=0.95) of estimated PWV’s variance. Age alone explained 90% (R²=0.90).

Resting heart rate was 62±9 bpm and blood pressure was 125±11/70±7 mmHg in the AGBRESA bedrest study. Estimated PWV was 5.8±1.1 m/s and measured PWV was 4.8±0.6. Age and estimated PWV were highly correlated (R² 0.88, p<0.001, Figure 1A). The correlation between measured PWV and age was weaker (R² 0.55, p<0.001). In a quadratic regression model, age (beta-value 0.99, p<0.001) but not body-mass-index, sex, or mean arterial pressure predicted estimated PWV. The model explained 98% of estimated PWV’s variance. R² between estimated and measured PWV was 0.40 (p<0.05). We observed an increasing bias between estimated and measured PWV with advancing age with an average 0.96±0.83 m/s difference between methods (Figure 1B). When adjusting the correlation of measured and estimated PWV for age we could no longer observe a significant relationship (p=0.267).

To assess influences of entered rather than chronological age on estimated PWV, we repeated measurements in one male person, who is in his 50s and has normal BMI, and randomly changed the entered age in decades from 30-80 years.
We obtained measurements in each entered age decade thrice. Again, estimated PWV related to entered age ($R^2 = 0.996, p<0.001$, figure 1C) akin to the relationship between estimated PWV and chronological age in athletes and in bedrest-study participants.

Discussion

The idea of obtaining vascular measurements, such as PWV, is gaining insight in individual vascular risk above and beyond traditional risk factors. The clinical goal is to target preventive measures to patients most likely to benefit. Similarly to other studies, we observed an almost perfect correlation between estimated PWV and age in two independent cohorts. Strikingly, estimated PWV in elite master athletes, which would be expected to benefit from life-long exercise, and in healthy bedrest study participants of average physical fitness were located on the same regression line. Suffice it to say that many athletes were frustrated when we reported their findings.

Theoretically, our findings could result from methodological limitations of PWV estimates or a rather limited effect of lifelong exercise on aortic stiffness. A previous study showed significantly lower measured PWV in endurance trained compared to sedentary older men making a methodological limitation more likely. Indeed, in our study, estimated PWV substantially overestimated PWV, particularly in older persons. Moreover, the modest correlation between estimated and measured PWV was attenuated after adjusting for age in our relatively small bedrest cohort. Finally, in a previous study, estimated PWV highly correlated with PWV calculated solely from age and blood pressure. Thus, the algorithm providing PWV estimates appears to weigh age so strongly that subtle influences on vascular wall properties caused by hemodynamic changes and physical training cannot be discerned. Even more so, estimated PWV mainly reflects data entered prior to measuring blood
pressure rather than true vascular properties. The clinical implication is that estimated PWV is no substitute for measured PWV, which likely limits the utility the methodology in individualizing risk assessment. In fact, simply asking the patient in front of us for his or her age and measuring blood pressure provides almost as much information as estimating PWV. Instead, vascular ageing assessment using established methodologies rather than estimates should be considered 10.

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Disclosures
We declare no conflict of interest.


**Figure 1 A-C**

Comparison of two different methodologies to assess pulse wave velocity (PWV) in two different cohorts.

1A: Correlation between estimated PWV and age in 129 Masters Athletes (empty circles) and in 24 AGBRESA-study participants (black squares).

1B: Regression analysis between the measured PWV and estimated PWV difference with age in 24 AGBRESA-study participants. Estimated deviated from measured PWV with increasing age ($R^2$ 0.44, p=0.07).

1C: Quadratic regression analysis between estimated PWV and entered age in one man being in his 50s. We randomly entered age in decades from 20-80 and obtained measurements thrice at each entered age.
A Correlation of estimated PWV with Age in two independent cohorts

Independent cohorts

- Masters Athletes $R^2$ quadratic 0.92
- AGBRESA $R^2$ quadratic 0.88
- Both cohorts $R^2$ quadratic 0.94

B Correlation of Delta-PWV (measured - estimated) with Age

Mean of Differences -0.96 | SD 0.83 m/s

$R^2$ quadratic of Delta-PWV versus Age 0.44

C Correlation of estimated PWV and Age in a single subject with randomly assigned age

$R^2$ quadratic 0.996