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Reproducibility and Impact of CT-Scanning on Pulse Wave Velocity Measurement for Cardiovascular Risk Stratification in an Asymptomatic Population

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Abstract

Objective: Pulse wave velocity (PWV) measurements for aortic arterial stiffness and coronary CT angiography (CCTA) may help improve cardiovascular risk assessment in asymptomatic people. On the CT-table PWV measurement is an efficient addition to the CT workflow. This study evaluated if on CT-table PWV measurements are influenced by CT anticipation stress and if the PWV measurements are reproducible.

Methods: Aortic PWV measurement reproducibility was assessed in 41 asymptomatic male sportsmen (aged 56.5 ± 6.7 years) who underwent CCTA as part of a sports medical evaluation. Three consecutive measurements were performed, two outside the CT-room for intra-observer variability followed by one on the CT-table. Pearson correlation coefficients were assessed for agreement between measurements outside the CT-room and on the CT-table. Bland-Altman analysis of limits of agreement was assessed to evaluate intra-observer variability outside the CT-room.

Results: Aortic PWV and systolic blood pressure (SBP) on the CT-table were significantly higher (+0.61 m/s, P = 0.004 and + 7 mmHg, P = 0.003 respectively), with acceptable correlation (Pearson's correlation 0.8, R^2 0.6). The Pearson's correlation coefficients of PWV measurements outside the CT-room showed good intra-observer agreement, (Pearson's correlation 0.9, R^2 0.8) The mean re-test difference and the 95% limits of agreement outside the CT-room were fair: 0.25 m/s, 95%CI -0.99–1.51 m/s.

Conclusion: On the CT-table PWV measurements, although higher due to anticipation stress causing higher SBP, are comparable to off-table measurements at rest. The reproducibility of PWV measurements is good when done prior to a coronary CT-scan and the limits of agreement are acceptable.

Keywords: Arterial stiffness; Aortic pulse wave velocity; Arteriograph; Oscillometric method; Cardiovascular risk stratification

Introduction

Traditional risk scores (e.g. the Framingham Heart Study score and ESC Systematic COronary Risk Evaluation (SCORE)) are used to estimate cardiovascular event risk in asymptomatic persons, aiming to divide them in low, intermediate and high risk categories. This corresponds to a 0-4%, 5-9% and 10% or higher 10 year cardiovascular mortality risk respectively, in case SCORE is used [1]. Cardiovascular risk scores do not account for past exposure to risk factors and physical activity of these persons, which will favorably influence their cardiovascular risk (e.g. by reduction of weight and blood pressure, and improving the lipid profile). It has been suggested that traditional cardiovascular risk scores underestimate the coronary artery calcium burden in persons who are physically active [2].

The coronary artery calcium score is the most powerful cardiac risk prognosticator in the asymptomatic population, with consistent superiority to all risk factor-based scores [3], an additional practical tool to assess more systemic arterial disease is measuring arterial stiffness of the aorta using pulse wave velocity (PWV) [4]. PWV has recently emerged as a potential new biomarker for prediction of cardiovascular mortality independent of established risk factors such as blood pressure and cholesterol [5-7], and can now be measured reliably and easily [8]. Moreover, the additive value of PWV to traditional risk factors, including Framingham risk score and SCORE, has been quantified in a number of studies [7,9]. In addition, a recent meta-analysis demonstrated that PWV has the ability to predict future cardiovascular risk and improves risk classification, adjusting for established risk factors [10].

Several PWV methods are available with SphygmoCorTM and ComplierTM being widely used to determine PWV, although both methods are observer-dependent and time-consuming [11]. A new investigator independent device using an oscillometric occlusive technique (ArteriographTM TensioMed Ltd, Budapest, Hungary) [8], shows comparable results to tonometry (ComplierTM) in healthy controls and patients with cardiovascular disease [12], and has recently been validated against the abovementioned tonometric and piezo-

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electronic methods that are clinically validated and widely accepted [8,12,13].

PWV measurements only take a few minutes and are usually performed after a few minutes of rest in an out-patient setting. PWV is can also be a practical measurement prior to coronary CT angiography (CCTA), as it provides additional information of systemic arterial disease. Blood pressure and heart rate measurement are standard procedures before acquiring CCTA and the Arteriograph with a blood pressure cuff can provide these standard measurements as well as PWV and other measurements in a fast and efficient way. Ideally one would prefer conducting these measurements after minutes of rest in a quiet room near the CT room. This is however time-consuming, as the subject must undress twice and move between two rooms, with extra personnel required to manage both rooms. On the CT-table measurement, just prior to CT scanning, is more efficient and cheaper. However, PWV measurements may be influenced by the anticipation stress of undergoing a CCTA. This study aimed to assess if PWV measurements using the Arteriograph on the CT-table directly prior to undergoing CCTA correlate well with PWV measurements outside the CT-room in a restful setting . A secondary aim was to compare two baseline PWV measurements outside the CT-room for intra-observer agreement.

Materials and Methods

Ethics statement

This study, with medical ethics committee of the University Medical Center Utrecht approval, complies with the Declaration of Helsinki, and all participants gave written informed consent.

Aortic PWV was measured non-invasively using an Arteriograph in 41 asymptomatic males who underwent CCTA (256-slice Philips Healthcare) as part of a sports medical evaluation. Exclusion criteria were contraindications for contrast-agents, renal insufficiency or known cardiovascular disease. In a room adjacent to the CT-room the oscillometric PWV pressure curves, brachial blood pressure (mm Hg) and heart rate (beats per minute) were measured in the left arm using a blood pressure cuff after several minutes of supine rest. Estimation of the distance travelled by the pulse wave, based on the tape-measured distance between the sternal notch and symphysis, was measured once. One operator performed three consecutive PWV measurements within one hour in each participant. Two sequential measurements outside the CT-room, separated by a 2-minute interval, were obtained for intra-observer agreement (linear regression analysis and Pearson's correlation coefficient), and the mean was used to compare to a third measurement on the CT-table directly prior to the CCTA examination (situation dependency). Reproducibility was assessed using the Bland-Altman method, paired samples t-test, R2, and Pearson coefficient (normalized covariate correlation coefficient). Values of P less than <0.05 were considered statistically significant.

Results

The clinical characteristics and hemodynamic parameters of the subjects are shown in Table 1. Measurements were performed in 41 men aged 47–68 years (mean 56.5 ± 6.7). Baseline characteristics: height 182.3 ± 8.0 cm; weight 84 ± 11 kg; BMI 25 ± 3.9kg/m^2; heart rate 58 ± 10 bpm; systolic 126 ± 16 mmHg and diastolic blood pressure 77 ± 11 mmHg. The mean aortic PWV measurement was 8.13 ± 1.4 m/s (range 6.15-13.1) outside the CT-room, and 8.74 ± 1.94 m/s (range 6.9-15.4) on the CT-table. The correlation coefficients for agreement between measurements outside the CT-room and on the CT-table are presented in Figure 1.

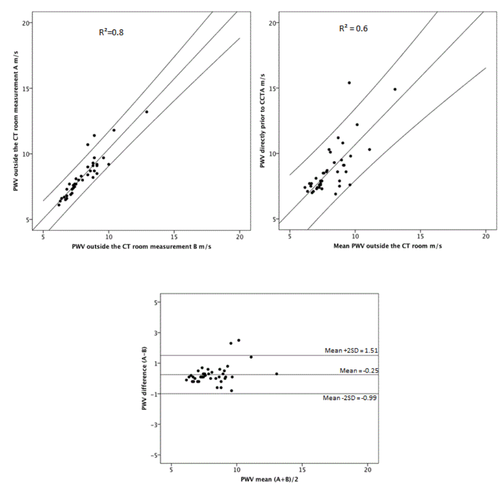

Figure 1: Intra-observer linear regression analysis, situation dependency linear regression analysis and levels of agreement

The correlation of the measurements outside the CT room was good (Pearson's correlation 0.9. R^2 of 0.8). No systematic bias was observed outside the CT-room, the mean difference was acceptable with 0.25 m/s, however, the 95% limits of agreement were higher than expected (-0.99–1.51 m/s). On CT-table pulse wave velocity as well as systolic blood pressure were significantly higher (+0.61 m/s, P = 0.004 and + 7 mmHg, P = 0.003 respectively), than measurements outside the CT-room with acceptable correlation (Pearson's correlation 0.8 and R^2 0.6). The heart rate was not significantly different between measurement outside the CT-room and on the CT-table.

Discussion

This study shows that PWV measurements are reproducible outside the CT-room in a restful setting and correlate reasonably well with PWV measurements on the CT-table. However, PWV results on the CT-table just before undergoing CCTA are significantly higher compared to outside the CT-room. This is probably caused by the rise in systolic blood pressure as a result of anticipation stress.

The correlation values outside the CT-room are similar to those reported previously [13,14]. Moreover, Horvath et al. [8], showed significant correlation between the invasively measured true aortic PWV and PWV determined by oscillometry, with acceptable limits of agreement for clinical practice. These correlations were better than earlier studies where aortic PWV values were compared to more time-consuming carotid-femoral PWV techniques [11,13].

The variance between our two measurements outside the CT-room was slightly higher than reported previously by Baulmann et al. (0.25 m/s versus 0.18 m/s) but lower than for the broadly accepted tonometric and piezo-electronic systems (0.36 and 0.31 respectively) [15].

The present study has several limitations. First of all the Arteriograph is a relatively new device for the assessment of PWV. To date, no prospective outcome studies have been carried out with this device. Although we chose to test PWV in a CT setting, ideally, the Arteriograph should be implemented in the outpatient setting, such as during a sports medical evaluation. Our study shows that the systolic blood pressure was significantly higher on the CT-table whereas blood pressure is also a major determinant of aortic PWV and is affected by stress such as the surrounding environment like the CT-room. Therefore, on-table aortic-PWV measurements probably overestimate the real potential risk estimation somewhat when (anticipation) stress is not kept in mind. Furthermore, we only performed measurements in a relatively small group, which also prevents us from providing any results on correlation with CAD findings on CCTA. Finally, measuring the distance between the jugular fossa and the symphysis is subject to error. However, we chose not to test this and used the same distance for the intra-observer agreement as well as for the situation independency.

Our results indicate that PWV is an efficient method with simple instructions that can give reproducible results. This supports the inclusion of Arteriograph in large-scale studies as a simple, non-invasive method for the assessment of arterial stiffness, a more systemic marker of arterial disease than focusing only on the coronary arteries. Ultimately, such studies may improve our understanding of cardiovascular disease and improve risk stratification. Additionally the next step of validation of Arteriograph PWV measurement would be to evaluate the Arteriograph PWV measurements and CCTA in a larger group and acquire more clinical evidence that the Arteriograph can provide additional prognostic value for cardiovascular disease risk assessment.

Conclusion

On the CT-table PWV measurements are efficient, and, although higher due to anticipation stress, do correlate with off-table measurements in a restful setting. The reproducibility of aortic PWV measurements using a simple blood pressure cuff oscillometer is good when done prior to a coronary CT-scan with fair limits of agreement. Future studies in a larger population are required to test the validity and usefulness of arterial stiffness measurements in combination with coronary CT.

Conflict of Interest

The authors declare that there is no conflict of interest

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Ethical Approval

This study has been approved by the regional Medical Ethics Committee (VCMO, Nieuwegein, The Netherlands, Ethics Committee reference number NL38234.100.11 R-11.44M/MARC). Subsequently, the local ethics board committee of the University Medical Center Utrecht, The Netherlands, approved this study. The study is conducted according to the principles of the Declaration of Helsinki and in accordance with the Dutch Medical Research Involving Human Subjects Act. Participants were only included after written informed consent was obtained.

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