Investigating the Association of Relative Central Blood Pressure Indices and Severity of Coronary Artery Disease

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Abstract

Background: Central blood pressure is an important index in central hemodynamic stress and may be associated with an increased risk of cardiovascular diseases.

Objectives: This study evaluated the central blood pressure indices in coronary artery disease (CAD) subjects and their association with the number of diseased vessels involved in CAD.

Methods: A random sample of 300 Iranian subjects who underwent coronary angiography (mean age 58.08 ± 10.62 years) was studied. Coronary lesions were defined as luminal stenosis ≥ 50% and the number of diseased vessels and the central aortic pressure were taken. The probability of central blood pressure indices with the number of diseased vessels was also determined by using cut-off points, based on the sensitivity, specificity, positive predictive value, and negative predictive value.

Results: The central blood pressure indices (fractional pulse pressure (FPP), systolic pressure (FSP), diastolic pressure (FDP) and FSP/FDP) were statistically significant in CAD patients with an increase in the number of diseased vessels (P < 0.001). There was a significant association between central blood pressure indices and CAD (P < 0.001) as well as with the increase in the number of diseased vessels (P < 0.001). Both odds ratio (11.84; 95% CI: 6.11 - 22.95; P < 0.001) and ROC analysis (AUC: 0.909; 95% CI: 0.870 - 0.939; P < 0.001) showed FSP as the strongest predictor of CAD. Furthermore, cut-off points of the FSP (≥ 1.373), FDP (≤ 0.811), FPP (≥ 0.559) and FSP/FDP (≥ 1.688) were determined for CAD for the first time based on 92% sensitivity, and 74% specificity.

Conclusions: FDP, FSP, and FSP, in particular, could be the effective predictors of CAD in Iranian populations. Therefore, the quality of life may be improved by the management of central blood pressure and using CAD cut-off points.

Keywords: Coronary Angiography, Blood Pressure, Coronary Artery Disease, Aortic Pressure

1. Background

Coronary artery disease (CAD) is one of the major causes of mortality and morbidity in industrial societies, for which there are many risk factors (1). Age, sex, smoking, dyslipidemia, diabetes mellitus and hypertension are associated with the severity of coronary lesions in angiography (2). Increased brachial blood pressure is one of the most important risk factors for cardiovascular events in the future. However, the brachial blood pressure does not accurately reflect central aortic blood pressure, as it may indicate a false increase in isolated peripheral systolic blood pressure despite normal aortic blood pressure (3). However, some studies have demonstrated that more than 30% of men and 10% of women with normal brachial blood pressure had central blood pressure similar to individuals with stage 1 hypertension (4). New evidence suggests the central blood pressure may predict cardiovascular events and end-organ damage associated with hypertension better than the brachial pressure (5-7).

Central blood pressure is a useful index for central hemodynamic stress and may be associated with an increased risk of cardiovascular diseases. Moreover, central blood pressure is suggested as a more reliable marker for cardiovascular events rather than the brachial pressure measurement (3, 8). However, the relationship between central blood pressure parameters and the severity of coronary artery disease has not been well addressed (3, 9). Central aortic pressure indices such as pulse pressure (PP), fractional systolic pressure (FSP) and fractional diastolic pressure (FDP) may be associated with an increased risk of cardiovascular disease. Additionally, according to studies, the severity of coronary artery disease can be predicted by...
measuring FSP and FDP. Furthermore, a higher central PP is associated with extensive CAD in angiography.

2. Objectives

This study aimed to assess the relationship between the severity of coronary artery disease and central aortic blood pressure. Moreover, the probability of CAD and 3VD has been determined for the first time by using cut-off points based on sensitivity, specificity, NPV, and PPV in an Iranian population.

3. Methods

3.1. Study Population

This study was a hospital-based cross-sectional study conducted at the Center for Elective Diagnostic Coronary Angiography, Ahvaz, Iran. The study population included a total of 300 subjects within an age range of < 18 years old, who were selected, based on the simple random sampling method and the following selection criteria from December 2017 to December 2018.

3.2. Selection Criteria

Patients with the following conditions were excluded from this study: no sinus rhythm, aortic valve stenosis or regurgitation more than mild severity and other valves more than moderate severity, renal impairment with 1.5 < serum creatinine, peripheral artery disease, CABG cases, and contraindications of coronary artery angiography. Moreover, patients who had MI or thromboembolism in the last three months were excluded from the study to prevent any interference with the analysis results. Informed written consent was obtained from all subjects. The study was approved by the ethical review board at Ahvaz University of Medical Sciences (ethical ID number: IR.AJUMS.REC.1397.016).

3.3. Data Collection and Central Blood Pressure Measurements

The main risk factors of CAD were extracted for all patients, based on history, examination, and medical record data. After which they underwent angiography. The central aortic blood pressure of the patients was measured during angiography. An angiographic catheter was placed in an ascending aorta and connected to a pressure transducer with a fluid-filled system to measure central systolic blood pressure (SBP) and central diastolic blood pressure (DBP).

Mean arterial pressure (MAP) and arterial pulse pressure (PP) were obtained to calculate FSP, FDP and FPP, which were FSP = SBP/MAP, FDP = DBP/MAP, FPP = PP/MAP, respectively.

3.4. Determine the Number of Diseased Vessels

The severity of coronary artery disease was also calculated by the cardiologist, and the results were divided into two groups: NO CAD and CAD. The CAD cases were then classified based on the severity of CAD with more than 50% stenosis in the form of one vessel disease (1VD), two-vessel disease (2VD), and three-vessel disease (3VD).

3.5. Statistical Analysis

In order to determine the significance of different parameters, the data collected during the current study were recorded and statistically analyzed by the SPSS program (version 22.0) and Medcalc (version 15.0). Results were expressed as mean ± SD. The Kolmogorov-Smirnov test and Q-Q plot were used to study the normality of the data.

Univariate data analysis was conducted using an independent t-test, ANOVA test, and Spearman correlation coefficient. Multivariate data analysis was carried out using ordinal regression and logistic regression. Moreover, the ROC curve was used to assess the diagnostic power of variables, and the appropriate cut-off points were obtained based on sensitivity, specificity, positive predictive value, and negative predictive value. The significance level was considered to be 0.05.

4. Results

Out of 300 subjects, the coronary artery angiography of whom was recorded, 211 patients (59.6 years ± 9.6) were classified as CAD and 89 individuals (54.45 years ± 11.9) as NO CAD. There were 163 (54.3%) males and 137 (45.7%) females (data not shown). The mean relative indices of central blood pressure (FPP, FSP, FDP, and FSP/FDP) in NO CAD patients and patients with 1VD, 2VD, and 3VD are presented in Table 1. There were significant differences in all central blood pressure indices in these groups (P < 0.001).

Odds ratio (OR) for the FPP, FSP, FDP, and FSP/FDP was found to be significant (P < 0.001) in CAD and 3VD subjects (Table 2). According to ordinal regression analysis in which variables such as age and sex were matched, there was a relationship between the relative indices of central blood pressure and the number of diseased vessels such that the higher the number of diseased vessels, the higher the FPP, FSP, FDP and the lower the FDP (P < 0.001) (Table 3).

The ROC curve was used to evaluate the predictive power of central blood pressure indices (Table 4). The ROC curve for SBP, DBP, FPP, FSP, FDP and FSP/FDP was 0.672, 0.757, 0.909, 0.909, 0.909, and 0.909 for CAD diagnosis, respectively. All central blood pressure indices (especially relative indices) had predictive power for CAD diagnosis (P <
Table 1. Comparisons of the Relative Indices of Central Blood Pressure in NO CAD Patients and the Number of Coronary Artery Disease (1VD, 2VD, 3VD)

|                      | NO CAD   | CAD (1VD, 2VD, 3VD) | 1VD       | 2VD       | 3VD       | P Value* |
|----------------------|----------|---------------------|-----------|-----------|-----------|----------|
| FPP                  | 0.52 ± 0.10 | 0.76 ± 0.14         | 0.62 ± 0.11 | 0.74 ± 0.10 | 0.88 ± 0.09 | < 0.001  |
| FSP                  | 1.34 ± 0.07 | 1.50 ± 0.09         | 1.41 ± 0.07 | 1.49 ± 0.06 | 1.59 ± 0.06 | < 0.001  |
| FDP                  | 0.82 ± 0.03 | 0.74 ± 0.04         | 0.79 ± 0.03 | 0.75 ± 0.03 | 0.70 ± 0.03 | < 0.001  |
| FSP/FDP              | 1.63 ± 0.16 | 2.04 ± 0.27         | 1.80 ± 0.19 | 2.00 ± 0.19 | 2.26 ± 0.19 | < 0.001  |

Abbreviations: CAD, coronary artery disease; FDP, fractional diastolic pressure; FPP, fractional pulse pressure; FSP, fractional systolic pressure; 1VD, one vessel disease; 2VD, two vessel disease; 3VD, three vessel disease

*P Value: comparison between NO CAD and CAD

Table 2. Odds Ratio According to the Relative Indices of Central Blood Pressure for the Diagnosis of CAD (vs. NO CAD Patients) and the Occurrence of 3VD (vs. the Total Patients with 1VD and 2VD)

|                  | OR (%95 CI) | P Value |
|------------------|-------------|---------|
| CAD              |             |         |
| FSP/FDP          | 2.76 (2.09, 3.64) | < 0.001 |
| FPP              | 5.20 (3.14, 8.08) | < 0.001 |
| FSP              | 11.84 (6.11, 22.95) | < 0.001 |
| FDP              | 0.007 (0.002, 0.03) | < 0.001 |
| 3VD              |             |         |
| FSP/FDP          | 2.28 (1.82, 2.85) | < 0.001 |
| FPP              | 4.85 (3.15, 7.47) | < 0.001 |
| FSP              | 10.68 (5.59, 20.43) | < 0.001 |
| FDP              | 0.009 (0.002, 0.032) | < 0.001 |

Abbreviations: CAD, coronary artery disease; CI, confidence interval; FDP, fractional diastolic pressure; FPP, fractional pulse pressure; FSP, fractional systolic pressure; OR, odds ratio; 1VD, one vessel disease; 2VD, two vessel disease; 3VD, three vessel disease

Table 3. Association of Relative Indices of Central Blood Pressure and the Number of Coronary Arteries Disease (0 = No CAD, 1 = 1VD, 2 = 2VD, 3 = 3VD) Matched for Age and Gender by Linear Regression Models

|                  | β          | %95 CI     | P Value |
|------------------|------------|------------|---------|
| FSP/FDP          | 9.227      | (7.792, 10.662) | < 0.001 |
| FPP              | 16.22      | (13.71, 18.71) | < 0.001 |
| FSP              | 24.32      | (20.59, 28.06) | < 0.001 |
| FDP              | -48.65     | (-56.12, -41.18) | < 0.001 |

Abbreviations: β, ordinal regression coefficient; CAD, coronary artery disease; CI, confidence interval; FDP, fractional diastolic pressure; FPP, fractional pulse pressure; FSP, fractional systolic pressure; 1VD, one vessel disease; 2VD, two vessel disease; 3VD, three vessel disease

Table 4. The AUC of the Relative Indices of Central Blood Pressure for the Diagnosis of CAD (vs. NO CAD Patients) and the Occurrence of 3VD (vs. the Total Patients with 1VD and 2VD) Using the ROC Curve

|                  | AUC (%95 CI) | P Value |
|------------------|--------------|---------|
| CAD              |             |         |
| SBP              | 0.672 (0.616, 0.725) | < 0.001 |
| DBP              | 0.757 (0.704, 0.804) | < 0.001 |
| FSP/FDP          | 0.909 (0.870, 0.939) | < 0.001 |
| FPP              | 0.909 (0.870, 0.939) | < 0.001 |
| FSP              | 0.909 (0.870, 0.939) | < 0.001 |
| FDP              | 0.909 (0.870, 0.939) | < 0.001 |
| 3VD              |             |         |
| SBP              | 0.679 (0.61, 0.741) | < 0.001 |
| DBP              | 0.676 (0.609, 0.739) | < 0.001 |
| FSP/FDP          | 0.894 (0.845, 0.932) | < 0.001 |
| FPP              | 0.894 (0.845, 0.932) | < 0.001 |
| FSP              | 0.894 (0.845, 0.932) | < 0.001 |
| FDP              | 0.894 (0.845, 0.932) | < 0.001 |

Abbreviations: AUC, area of ROC curve; CAD, coronary artery disease; CI, confidence interval; FDP, fractional diastolic pressure; FPP, fractional pulse pressure; FSP, fractional systolic pressure; 1VD, one vessel disease; 2VD, two vessel disease; 3VD, three vessel disease

0.001). Moreover, the ROC curve for central blood pressure indices and the predictive power of the main 3VD was 0.679, 0.676, 0.894, 0.894, 0.894, and 0.894, respectively. Thus, it can be concluded that central blood pressure indices have predictive power for an increase in the number of diseased vessels (P < 0.001). This diagnostic power of 3VD in CAD patients for relative indices of central blood pressure (FPP, FDP, FSP, FSP/FDP) is higher than that of absolute indices (SBP, DBP).

Regarding the significant relationship between central blood pressure indices, CAD and 3VD, two cut-off points were determined; once with high sensitivity and the next time with high specificity, positive predictive value (PPV) and negative predictive value (NPV) at both cut-off points (Table 5). For example, the cut-off point of the FSP index for CAD group (all patients with 1VD, 2VD, and 3VD) was ≤ 1.373 based on 92% sensitivity, and 74% specificity. Another cut-off point of the same index was ≤ 1.421 with a sensitivity of about 77%, but a specificity of about 93%.
### Table 5. Cut-Off Points of Relative Indices of Central Blood Pressure for Diagnosis of CAD and 3VD Based on Sensitivity, Specificity, Positive Predictive Value, and Negative Predictive Value

| Cut Points | FSP/FDP | FPP | FSP | FDP |
|------------|---------|-----|-----|-----|
| CAD        | ≥ 1.688 | ≥ 0.559 | ≥ 1.373 | ≤ 0.811 |
|            | 91.94 (87.4, 95.2) | 74.16 (61.8, 82.9) | 89.4 (84.5, 93.2) | 79.5 (69.2, 87.6) |
|            | ≥ 1.800 | ≥ 0.632 | ≥ 1.421 | ≤ 0.787 |
|            | 72.25 (71.0, 82.7) | 93.26 (85.9, 97.5) | 96.4 (92.4, 97.7) | 61.4 (54.5, 71.6) |
| 3VD        | ≥ 2.000 | ≥ 0.750 | ≥ 1.500 | ≤ 0.740 |
|            | 86.08 (76.5, 92.8) | 79.55 (71.7, 86.1) | 71.6 (61.4, 80.4) | 90.5 (83.7, 95.2) |
|            | ≥ 2.154 | ≥ 0.833 | ≥ 1.556 | ≤ 0.720 |
|            | 69.62 (58.2, 79.5) | 87.88 (81.1, 92.9) | 77.5 (66, 86.5) | 82.9 (75.6, 88.7) |

Abbreviations: CAD, coronary artery disease; CI, confidence interval; FDP, fractional diastolic pressure; FPP, fractional pulse pressure; FSP, fractional systolic pressure; NPV, negative predictive value; PPV, positive predictive value; SN, sensitivity; SP, specificity; 3VD, three vessel disease.

### 5. Discussion

Studies have been conducted on central aortic blood pressure indices such as FPP, FSP and FDP, and their association with cardiovascular outcomes, confirming the association of these indices with the increased risk of cardiovascular disease and an increase in the severity of coronary artery disease (10, 12, 13). Previous studies have reported the association between central blood pressure and cardiovascular diseases (3, 5, 6). Moreover, Jankowski et al. showed that PP, FSP, and FDP of the central aorta were associated with the risk of 3VD in CAD patients. They stated that the risk of 3VD increases by 15%, 28%, and 39% per 10 mmHg increases in the central PP, per 0.1 increases in FSP and per 0.1 reductions in FDP, respectively (14). As observed in this study, there was a significant association between increased FPP, FSP and FSP/FDP, decreased FDP, and the higher risk of 3VD (FPP ≥ 1.373, FDP ≤ 0.811, FSP ≥ 0.559) and FSP/FDP (≥ 1.688) for CAD were determined in this study based on 92% sensitivity and 74% specificity. Additionally, cut-off points of FSP (≥ 1.500), FDP (≤ 0.740), FSP (≥ 0.750) and FSP/FDP (≥ 2.000) were determined for 3VD with 86% sensitivity and 80% specificity.

#### 5.1. Conclusions

Central blood pressure indices, such as FPP, FDP, FSP, FSP/FDP may be associated with increased diseased vessels in CAD. However, FSP has been shown as the strongest predictor of CAD in Iranian populations. Therefore, the quality of life may be improved by the management of blood pressure treatment based on central blood pressure control and using cut-off points.

#### 5.2. Study Limitations

1. There were a limited number of patients, and we used a small group who were referred for elective CAG.

2. A fluid-filled system was used to record coronary BP, while the use of a high-fidelity pressure transducer can increase the accuracy of the recorded pressure in this study. So, high-fidelity pressure transducer might be used as an advanced pressure measurement device in future clinical studies.
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Footnotes

Authors’ Contribution: Study concept and design: Pouria Ali Forouzanmehr and Ebrahim Haidary Sardaby. Analysis and interpretation of data: Pouria Ali Forouzanmehr. Drafting of the manuscript: Pouria Ali Forouzanmehr. Critical revision of the manuscript: Pouria Ali Forouzanmehr, Ebrahim Haidary Sardaby, and Saeed Hesam. Statistical analysis: Saeed Hesam.

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Patient Consent: Informed written consent was obtained from all subjects.

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