Prevalence and clinical characteristics of pseudohypertension in elderly patients prepared for coronary artery angiography

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Abstract
Background: Pseudohypertension (PHT) can cause adverse effects in the elderly owing to administration of antihypertension therapy. The present study aimed to determine the prevalence of PHT in the elderly and associated risk factors to investigate a noninvasive method of detection of PHT.

Methods: We recruited 151 patients (age ≥60 years) who underwent coronary angiography. Demographic and clinical data were collected from the patients. During coronary angiography, intrabrachial arterial pressure and indirect blood pressure were measured. Brachial-ankle pulse wave velocity (ba-PWV) was measured within 2 weeks after coronary angiography.

Results: Based on the differences between the direct and indirect pressure measurements, the patients were divided into a PHT group (n = 87) and a non-PHT group (n = 64). The prevalence of PHT was 57.6%, and the development of PHT was significantly associated with older age. Serum creatinine level and creatinine clearance rate were significantly higher in the non-PHT group than in the PHT group (P < .05). In addition, the PHT group had significantly higher ba-PWV and pulse pressure (PP) than the non-PHT group (P < .05). Receiver-operating characteristic curve analysis revealed that ba-PWV (AUC = 0.783) and PP (AUC = 0.791) showed a relatively good diagnostic performance for PHT.

Conclusions: PHT was present in most of the elderly who had indications for coronary angiography and associated with age and renal function. The data from the present study also suggested that both PP and ba-PWV could be used to positively predict PHT.

Abbreviations: AUC = area under the curve, ba-PWV = brachial-ankle pulse wave velocity, ECG = electrocardiography, PHT = pseudohypertension, PP = pulse pressure, ROC = receiver-operating characteristic, SD = standard deviation.

Keywords: artery sclerosis, brachial-ankle pulse wave velocity, elderly, hypertension, pseudohypertension, pulse pressure

1. Introduction

Pseudohypertension (PHT) is mostly used to describe the condition in which brachial arterial pressure is assessed with a cutoff of 10 mm Hg or higher than the intra-arterial pressure assessed invasively. In 1892, William Osler described a condition that likely represented PHT.[1] However, it was not until 1974 that the term pseudohypertension first appeared in the medical literature.[2] Based on previous studies performed to compare between indirect and direct measurements, the prevalence of PHT was estimated to range from being quite rare (1.7%) to being rather common (>65%).[3] Owing to its clinical symptoms, PHT is an important hypertensive disease in the elderly.[4] Appropriate antihypertension therapy for patients with true hypertension could produce potentially adverse effects such as postural hypotension, dizziness, and even acute cardio-cerebrovascular events in patients with PHT. As the aging population of China increased, hypertension became a major challenge in the elderly, which accounts for approximately 49% of individuals aged > 60 years.[5] These population changes mean that thousands of patients are at risk of developing this condition.

The prevalence of PHT is difficult to estimate because of not only the varied definitions in the literature[6-9] and selection bias in the study cohort of patients already suspected with PHT[6-9] but also the lack of convenient, noninvasive, painless, and accurate methods to verify this condition. The invasive intra-arterial pressure measurement via arterial puncture is still the gold standard diagnostic method for PHT. After years of study, a stiff brachial artery wall has been well known to be a possible main cause for PHT.[2,10,11] Thus, patients who present with concomitant medical conditions of arteriosclerosis disease, chronic kidney disease, diabetes mellitus, hypertension, and hyperlipidemia are more likely to be susceptible to developing PHT because these conditions could affect vascular flexibility.

In the present study, we determined the prevalence of PHT among both hypertensive and normotensive patients, and identified the risk factors associated with the development of PHT. In addition, both brachial-ankle pulse wave velocity (ba-PWV) and pulse pressure (PP) are important parameters for estimating arterial stiffness. We also identified the role of ba-PWV and PP in the diagnosis of PHT. Our results could provide a reference for developing noninvasive methods for detection of PHT in the elderly.
2. Methods

2.1. Patient enrollment

The present cross-sectional study was performed in patients with or without hypertension who prepared to undergo coronary artery angiography in the Cardiology Department of Renji Hospital, Shanghai Jiao Tong University School of Medicine between September 2012 and May 2013. For enrollment, patients with or without hypertension should be aged ≥60 years and have stable vital signs. Patients with any of the following conditions were excluded: (1) presence of peripheral arterial disease, aorto-arteritis or renal insufficiency (serum creatinine level of ≥2.2 mg/dL), (2) the presence of significant arrhythmia such as persistent atrial fibrillation and frequent ventricular premature complexes, (3) receiving any blood purification therapy such as hemodialysis and peritoneal dialysis, (4) allergic reaction to iodinated contrast, and (5) the presence of 10 mm Hg or higher difference in cuff blood pressure between the two upper extremities in indirect blood pressure measurement.

After enrollment, the patients underwent a standardized interview and clinical examination. Demographic and clinical data in terms of age, sex, and history of medication were collected and recorded. Serum lipid profile, fasting and postprandial blood glucose levels, serum creatinine level, and uric acid level were measured and recorded from each patient within 2 days after hospital admission. Hypertension and its comorbidities were diagnosed as previously reported as follows[12]: hypertension, fasting glucose levels, serum creatinine level, and uric acid level were >7.8 mmol/L or glucose level of >11.1 mmol/L for 2 hours after oral glucose challenge; and dyslipidemia, with total cholesterol level of >6.5 mmol/L. Moreover, thoracic aortic disease was diagnosed in accordance with the Guidelines for the Diagnosis and Management of Patients with Thoracic Aortic Disease.[13] This study was authorized by the ethics committee of Shanghai Renji Hospital and all the included patients signed the informed consent agreement.

3. Blood pressure measurements

All the patients underwent coronary artery angiography via the transradial artery approach, and blood pressure was measured in the supine position during cardiac catheterizations. Following the completion of angiography, the guiding catheter was withdrawn from the brachial artery, followed by application of a pressure transducer (Abbott Critical Care Systems, Abbott, Ireland). When the blood-pressure reading settled, three blood pressure values were obtained through direct measurement. At the same time, blood pressure on the contralateral upper extremity was measured with an automated electrocardiography (ECG) monitor (IntelliVue MP50, Philips, China). All the patients underwent measurement of ba-PWV by using Form BP-203RPEIII (Omron-Colin, Tokyo, Japan) by the same technician, 2 weeks after undergoing coronary angiography. PHT was defined as a 10 mm Hg or greater pressure difference between the noninvasive and invasive cuff measurements via the brachial artery catheter.

4. Data analyses

Statistical Package for Social Sciences version 19.0 (SPSS Inc., Chicago, IL) was used for the statistical analysis in our study. Continuous variables were expressed as mean ± standard deviation (SD) (normally distributed variables), and an indepen-
PHT and non-PHT groups; thus, we further compared the creatinine clearance rate between the two groups. Consequently, we also found a significant difference in creatinine clearance rate (78.78 ± 22.01 mL/min vs 89.60 ± 26.66 mL/min, P = .007, Table 1).

Furthermore, we examined the association of the prevalence of PHT with both sex and age. As shown in Table 2, 151 patients were divided into three groups based on age distribution as follows: 60 to 65 years, 66 to 75 years, and ≥ 76 years. The results indicated that the prevalence of PHT increased significantly with age (60–65 years vs 66–75 years vs ≥ 76 years: 48.10% vs 62.96% vs 83.33%, P = .015) but not the gender (P = .213).

Moreover, we investigated the correlation of the difference in direct-indirect systolic pressure (S-S) with PP and ba-PWV by using the Pearson correlation coefficient. As displayed in Table 3, S-S significantly correlated to both PP (r = .385, P < .001) and ba-PWV (r = .320, P < .001). Meanwhile, age was remarkably correlated to both ba-PWV (r = .459, P < .001) and PP (r = .299, P < .001). Moreover, an obvious correlation was also identified between PP and ba-PWV (r = .400, P < .001). The diagnostic performance of PP and ba-PWV for PHT was assessed by using a ROC analysis, and the AUC of PP and ba-PWV for detection of PHT were 0.791 and 0.783, respectively (Fig. 1). In addition, the ROC analysis of PP revealed that the cutoff value of 1721.5 cm/s had a sensitivity of 79.3% and a specificity of 73.4% for detecting PHT.

### Table 2
Incidence of PHT associated with both gender and age among patient with resistant hypertension.

| Gender       | Number of PHT/total number (%) | P value |
|--------------|--------------------------------|---------|
| Male         | 55/89 (61.80%)                 | .213    |
| Female       | 32/62 (51.61%)                 |         |
| Age          |                                |         |
| 60–65 years  | 38/79 (48.10%)                 | .015    |
| 66–75 years  | 34/54 (62.96%)                 |         |
| ≥ 76 years   | 15/18 (83.33%)                 |         |

**Table 3**

Correlation among S-S, age, PP, and ba-PWV.

|          | S-S   | Age   | ba-PWV | PP   |
|----------|-------|-------|--------|------|
| r value  | 1     | 0.203 | 0.320  | 0.385|
| P value  |       | .012  | .000   | .000 |
| r value  | 0.203 |       | 0.459  | 0.299|
| P value  | .012  |       | .000   | .000 |
| r value  | 0.320 | 0.459 |       | 1    |
| P value  |       | .000  |       | .400 |
| r value  | 0.385 | 0.299 | 0.400  |      |
| P value  | .000  | .000  |       |      |

**Table 4**

Correlation among S-S, age, PP, and ba-PWV.

|          | S-S   | Age   | ba-PWV | PP   |
|----------|-------|-------|--------|------|
| r value  | 1     | 0.203 | 0.320  | 0.385|
| P value  |       | .012  | .000   | .000 |
| r value  | 0.203 |       | 0.459  | 0.299|
| P value  | .012  |       | .000   | .000 |
| r value  | 0.320 | 0.459 |       | 1    |
| P value  |       | .000  |       | .400 |
| r value  | 0.385 | 0.299 | 0.400  |      |
| P value  | .000  | .000  |       |      |

**ba-PWV** = brachial-ankle pulse wave velocity, **PP** = pulse pressure, **S-S** = the difference of direct-indirect systolic pressure.

6. Discussion

The concept of PHT, which is caused by the possibility of overestimating brachial arterial pressure, has received considerable attention in the area of hypertension.[6,14–18] However, no consensus has been reached on the prevalence of PHT. Arterial stiffness is currently well known to be the main cause of the development of PHT. Elderly individuals are at high risk of PHT and receive inappropriate administration of hypertensive drugs because they are likely to have a stiff brachial artery.[4] To avoid the adverse effects caused by a misdiagnosed PHT, we conducted the present study to determine the prevalence of PHT in individuals with advanced age who underwent coronary angiography and identified a noninvasive method for detection of PHT. The main findings of the present study were as follows: (1) the prevalence of PHT in the elderly who underwent coronary angiography was 57.6% and the development of PHT was significantly associated with older age; (2) PHT was more likely associated with elevated serum creatinine levels compared with other risk factors that affect vascular compliance, such as blood glucose and lipid; (3) measurement of PP and ba-PWV as parameters of artery sclerosis has a relatively good diagnostic performance for detection of PHT, which could be used as a noninvasive method for predicting PHT, especially systolic PHT.

The discrepancy in the prevalence of PHT among elderly individuals could be attributed to several reasons.[6,9] First, the definition of PHT has several versions. The difference in cuff-to-intra-arterial pressure which could be referred as “PHT” ranged from 10 to 30 mm Hg.[6,9] Second, the patients recruited in these studies were at a relatively high risk for the developing PHT, such as those with the Osler maneuver, persistent hypertension without cardiomegaly, renal insufficiency, or funduscopic changes.[19] Data from the present study indicated that the prevalence of PHT was 57.6%. This high prevalence could be attributed to the patients recruited in the present study. These patients were evaluated with coronary angiography. Most of them had chest pain, palpitation, classic angina, or sclerosing vasculature. They had a high probability to develop a calcified...
brachial artery, which could lead to PHT. In addition, consistent with previous reports, the prevalence of PHT was significantly associated with the increase of age.\(^{[9]}\)

Based on the results of several previous studies, some risk factors have been suspected to be associated with the development of PHT, including arterial sclerosis, hyperlipidemia, elevated blood pressure and blood glucose, and increased level of serum creatinine.\(^{[10]}\) However, in the present study, blood pressure, and lipid and glucose levels were not correlated with the development of PHT.

The impaired renal function (increased serum creatinine and decreased creatinine clearance rate) was significantly associated with PHT. This result was consistent with those in several case reports of PHT in chronic renal failure and hemodialyzed patients with arteriosclerosis.\(^{[11,12]}\) suggesting that renal dysfunction might play an important role in the development of PHT. Patients with renal dysfunction frequently experience abnormal calcium and phosphate metabolisms. Disturbances in calcium and phosphate metabolisms can affect the formation of various soft tissues in patients, which lead to vascular calcification, which is considered the main mechanism of PHT.

Arterial stiffness contributes to the development of PHT. Various factors have been introduced to quantify the elastic properties of arteries. Among these factors, ba-PWV and PP are the two major indexes, especially ba-PWV, for evaluating the compliance of artery. Miwa et al.\(^{[13]}\) suggested that PP was the most powerful index for assessment of arterial compliance among three other parameters, including systolic, diastolic and mean blood pressures in the elderly individuals. With the advantages of user-friendly operation and easy application in the general population, ba-PWV was believed to be an identical predictor of arterial stiffness.\(^{[14,15]}\) In our study, both PP and ba-PWV were significantly correlated with PHT and presented a relatively good diagnostic performance for the detection of PHT.

Although our study provided important information on the development of PHT, it still has several limitations. First, the patients recruited in our study had symptoms, such as chest pain, that are suggestive of possible significant vascular diseases, which might result in higher morbidity of PHT. Second, ambulatory PP from ambulatory blood pressure monitoring might be a better way to assess PHT, as PP could be affected by fluctuation of blood pressure. Finally, the sample size was relatively small, and a large multicenter trial is still needed to confirm the findings of the present study.

7. Conclusion
The present study demonstrated that PHT is present in most elderly individuals who had indications for coronary angiography and was significantly associated with the increase in age and impairment of renal function. The data from the present study also suggested that both PP and ba-PWV could be used to positively predict PHT. However, a large multicenter trial is needed to confirm the findings of the present study.

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