Pulse Wave Velocity as a Measure of Arterial Stiffness in Patients with Abdominal Aortic Aneurysm: A Systematic Review and Meta-Analysis

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Abstract

Background and objective:
The relationship between pulse wave velocity (PWV) levels and abdominal aortic aneurysm (AAA) remains controversial. A meta-analysis was performed to establish whether vascular pulse wave velocity (PWV) as a measure of arterial stiffness is different in patients with abdominal aortic aneurysms and controls.

Methods

Pubmed, Embase, Cochrane and China National Knowledge Infrastructure (CNKI) were used for the meta-analysis with articles up to January 1, 2021. To compare PWV levels between AAA patients and healthy controls, pooled weighted mean difference (WMD) and its 95% confidence interval (CI) were calculated. Subgroup analysis and funnel plots are used to assess the quality of the combined results to ensure a normal distribution of data with minimal bias. Study quality for eligible studies was assessed using the Agency For Health Care Research and Quality (AHRQ) inventory tool.

Results

Nine cross-sectional studies, which included 439 abdominal aortic aneurysm cases and 382 healthy subjects, met inclusion criteria and were eligible for meta-analysis. We found that PWV levels were significantly higher [WMD(95%CI): 2.36(2.02,2.70)] in AAA patients than healthy controls. After subgroup analysis, it was found that age, sex, smoking and hypertension had significant effects on the PWV levels. The normal distribution of the Funnel plot analysis suggests a low risk for publication bias.

Conclusion

PWV levels were elevated in patients with AAA compared to healthy controls, with the effect on PWV altered by age, sex, smoking and hypertension. Our study suggests that abdominal aortic aneurysm is related to increased arterial stiffness.

Introduction

Abdominal aortic aneurysm (AAA) is defined as the localized dilatation of the aorta and is likely to rupture unexpectedly leading to serious morbidity and mortality [1, 2]. It is estimated that the incidence of AAA is about 4–8% in men and 1-1.3% in women and globally accounts for 168,200 deaths annually [3, 4, 5]. The primary mechanism by which AAA develop consists of chronic inflammation, vascular smooth muscle cell (VSMC) apoptosis, extracellular matrix (ECM) degradation, and thrombosis. [6, 7] Specifically, these factors are what contributes to atherosclerotic plaque formation, and hence atherosclerosis plays a significant role in forming AAA and plays a role in the aneurysmal wall formation. [8]

Atherosclerosis of arteries contributes to the loss of arterial elasticity, elevated arterial stiffness, and therefore increased PWV since pulse velocity travels faster in stiffened arteries. [9, 10] Arterial stiffness (AS), represented by the arterial wall rigidity, is one of the most available detectable manifestations of adverse structural and functional alterations within the arterial vessel wall. [11] Pulse wave velocity (PWV) is the velocity of a pulse wave moving through an arterial segment and is one of the non-invasive methods of assessing AS. [12, 13] The current literature on the differences between the PWV of AAA and controls is mixed. In some studies, PWV levels were significantly lower in AAA patients than those in healthy controls. [14] Contrarily, other studies have demonstrated that PWV levels in the abdominal aorta were significantly higher in AAA patients than those in non-AAA controls. [15, 16] Additional studies have failed to confirm either association of PWV levels with AAA. [17]

Based on the mixed literature in regards to the available evidence for pulse wave velocity and AAA incidence, we hypothesized that there may be a correlation between PWV levels and AAA. Therefore, we carried out a meta-analysis using published studies on PWV levels in AAA patients.

Material And Method

Database and Search Strategies

Our meta-analysis strictly followed the Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) guidelines [18].

We systematically searched PubMed, Embase, Cochrane Central Register of Controlled Trials, and the Chinese National Knowledge Infrastructure (CNKI database). The Medical Subject Headings (Mesh) and relevant keywords were used for literature research. The electronic literature search was complemented by a manual search of related articles. The reference lists of collected items were also manually reviewed for additional correlated articles.

PubMed search strategy was conducted using the following search field descriptions and tags; Title/Abstract [tiab] and MeSH Terms [MH]

#1."pulse wave velocity [mh]" OR "PWV [tiab]" OR "aPWV [tiab]" OR "cPWV [tiab]" OR "fPWV [tiab]" OR "cfPWV [tiab]" OR "arterial distensibility [tiab]" OR "vascular distensibility [tiab]" OR "aortic distensibility [tiab]" OR "arterial stiffness [tiab]" OR "arterial stiffening [tiab]" OR "vascular stiffness [tiab]" OR "vascular stiffening [tiab]" OR "aortic stiffness [tiab]" OR "aortic stiffening [tiab]" OR "arterial compliance [tiab]" OR "vascular compliance [tiab]" OR "aortic compliance [tiab]"
Inclusion and exclusion criteria of enrolled studies

Our inclusion criteria were as follows: the study had to be observational (i.e., a case-control, cross-sectional or cohort design); the subjects enrolled had to be diagnosed by the physician as AAA; there had to be comparison of vascular PWV between patients with AAA and controls without AAA; and PWV data had to be available for all patients. Exclusion criteria included: study had undefined control groups, duplicate or overlapped populations with a previous study, or PWV values were only reported in a single group and not both AAA and control.

Data extraction

Data were independently extracted from individual studies by two reviewers. Each study’s information was obtained using standardized forms by two independent observers blinded to the authors’ names and journal titles. Discrepancies between the outputs were resolved through discussion and involvement of a third co-author. The following information was extracted from each study (Table 1): (I) trial’s name/publication year; (II) numbers of subjects enrolled; (III) country; (IV) age; (V) male; (VI) BMI; (VII) outcome index; (VIII) PWV levels; (IX) device; (X) AHRQ scores; (XI) Smoking; (XII) Hypertension; (XV) diabetes.

Assessment of the risk for publication bias

This was conducted by two researchers independently. Because this meta-analysis included cross-sectional studies, study quality was assessed using the Agency For Health Care Research and Quality (AHRQ) inventory tool[19]. Eleven questions were answered. If the answer was "No" or "Unclear," the rating of the item was "1," if the answer was "Yes," the score of the item was "1." The quality for each study was scored as low (0-3), medium (4-7) or high (8-11). Studies graded as low quality (0-3) were excluded from the meta-analysis.

Statistical analysis

The meta-analysis was conducted using a synthesis dataset according to published eligible studies. Weighted Mean Difference (WMD) with corresponding 95% confidence interval (CI) was calculated to evaluate PWV and AAA correlations. If the $I^2$ value was > 50% with a $p<0.1$ for the test of heterogeneity, the results were considered heterogeneous.

Forest plots were used to display the results graphically. Further subgroup analysis based on anatomic location of PWV (carotid-femoral PWV and aortic PWV) was performed since some studies have argued that PWV in different locations of stiffened arteries varied unexpectedly. Additional subgroup analyses included age, sex, smoking, diabetes and hypertension. Subgroup analysis was also used to identify the factors contributing to the heterogeneity of the pooled data.

All reported P values were two-sided tests and considered statistically significant if $P <0.05$. Publication bias was assessed using funnel plots. All statistical analyses were performed by Stata 12.0 (Stata Corporation, College Station, TX, USA).

Results

Literature search

The literature and eligible studies are detailed in Figure 1. A preliminary electronic database search identified 244 potential records. After reviewing abstracts or full articles, 103 duplicate articles, 126 unrelated articles, 2 review articles, and 3 articles with unextractable data were excluded. In the end, nine studies qualified for the meta-analysis examining the association of PWV with AAA.

Study characteristics

The characteristics of included studies are presented in Table 1. 6 of which reported carotid-femoral PWV (cf-PWV) and 3 of which reported infrarenal arterial aortic PWV. Four studies reported data on both males and females, while 3 studies only reported data on males.

PWV measurement methods

Methods for PWV measurements varied among studies. 2 studies used a Complier SR, 2 studies used a SphygmoCor device, 2 studies used a Sonix RP system, and 3 studies used Electrocardiographically Gated 64-Detector Row CT.

Association of PWV levels with AAA

All 9 eligible studies reported on the relationship of PWV levels with AAA. As quantified using $I^2$ and $P$-value, the heterogeneity across included studies was statistically significant ($P<0.00001$, $I^2=98.9\%$). Studies were weighted based on the number of patients in each study and other factors. Meta-analysis showed that patient's PWV values were higher in patients with AAA than those in control subjects ($WMD=2.36\text{m/s}$, 95% CI $2.02\pm2.70$ [P=0.001]) (Figure 2A). To investigate potential publication bias, the funnel plot was created for studies included in a meta-analysis of PWV (Figure 2B), with a vertical axis for study size (standard error) and horizontal axis for the standardized difference in means which averaged overall at around 2.36. Lack of significant asymmetry in the funnel plot both on the x and Y axis in Figure 2B suggests the low likelihood of publication bias.

Subgroup analysis
Subgroup meta-analysis results are summarized in Table 2. High levels of pulse wave velocity were associated with AAA as defined by cf-PWV (WMD=0.63m/s,95% CI 0.26-1.00, P=0.000) and infrarenal PWV (WMD=12.65m/s,95% CI11.75-13.54, P=0.004) (Figure 3B).

Subgroup analysis was also performed if it was possible to match risk factors such as age (9/9 studies), sex (7/9 studies), smoking(6/9 studies), diabetes(5/9 studies) and hypertension(5/9 studies) (Table 2).

The PWV levels were significantly lower in AAA patients than those in the control group if there was significant inter-group difference in age between AAA and control (WMD=-0.48, 95%CI:-0.94,-0.01, I²=77%, P=0.005), however, PWV levels were significantly higher in AAA patients than those in the control group if there was not significant inter-group difference in age between AAA and control (WMD:5.59; 95%CI:5.09,6.09, I²=99%, P=0.000) (Figure 3B).

The PWV levels were significantly lower in AAA patients than those in the control group if there was significant inter-group difference in hypertension between AAA and control(WMD:-0.52,95%CI:-0.99,-0.06, I²=88.8%, P=0.003), however, PWV levels were significantly higher in AAA patients than those in the control group if there was not significant inter-group difference in hypertension between AAA and control (WMD:2.05; 95%CI:1.23,2.87, I²=96.7%, P=0.000) (Figure 4A).

The PWV levels were significantly lower in AAA patients than those in the control group if there was significant inter-group difference in diabetes between AAA and control(WMD:-2.10; 95%CI:-3.23,-0.97), however, PWV levels were significantly higher in AAA patients than those in the control group if there was not significant inter-group difference in diabetes between AAA and control (WMD:0.52;95%CI:0.11,0.93, I²=95.2%, P=0.000) (Figure 4B).

The PWV levels were not significantly different in AAA patients than those in the control group if there was significant inter-group difference in sex between AAA and control(WMD:-0.20; 95%CI:-0.71,0.31), however, PWV levels were significantly higher in AAA patients than those in the control group if there was not significant inter-group difference in sex between AAA and control (WMD:4.35;95%CI:3.89,4.80, I²=99.1%, P=0.000) (Figure 5A).

The PWV levels were significantly higher in AAA patients than those in the control group if there was significant inter-group difference in smoking between AAA and control(WMD:1.12; 95%CI:0.44,1.81), PWV levels were also significantly higher in AAA patients than those in the control group if there was not significant inter-group difference in smoking between AAA and control (WMD: 0.43;95%CI: -0.00, 0.87, I²=95.2%, P=0.000) (Figure 5B).

**Discussion**

This meta-analysis investigated whether vascular PWV levels as a measure of arterial stiffness is different in patients with abdominal aortic aneurysms compared to controls. A total of 9 cross-sectional studies met inclusion criteria for our analysis. Our results demonstrated that PWV levels in patients with AAA were significantly higher than those in controls, indicating the relationship between the abdominal aortic aneurysm and increased arterial stiffness.


In conclusion, our meta-analysis showed that PWV levels in AAA patients were significantly higher than those in control subjects. PWV value as a measure of arterial stiffness is changed in patients with abdominal aortic aneurysm and may be used to monitor disease progression. Our analysis warrants further investigation into the association of PWV levels with AAA disease in a more well-designed prospective cohort study.

**Declarations**

**Ethical Approval and Consent to participate**

Not applicable

**Consent for publication**

Not applicable

**Availability of data and materials**

Not applicable.

**Competing interests**

The authors declare that they have no competing interests

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**Authors’ contributions**

HLZ, YYS, TTC contribute to the conception and design of the study, HLZ, YYS, TTC, YZ, JTW, YKW, WJZ, GC, DLL, XXF, CX, BHX, JJJ and XFC contribute to analysis and interpretation of data, HLZ and XFC contribute to drafting the article, All of authors revise it critically for important intellectual content, and final approval of the version to be published.

**Acknowledgements**

Not applicable

**Authors’ information**

Not applicable

**References**


**Tables**

**Table 1:** Baseline characteristics
<table>
<thead>
<tr>
<th>Author/Year</th>
<th>n</th>
<th>Country</th>
<th>Age(year)</th>
<th>Male</th>
<th>BMI(kg/m²)</th>
<th>Case/control</th>
<th>Outcome index</th>
<th>PWV(m/s)</th>
<th>device</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abbas, A. et al 2015[17]</td>
<td>88</td>
<td>UK</td>
<td>AAA:73.1±5.7</td>
<td>46(100%)</td>
<td>27.1±4.2</td>
<td>46/42</td>
<td>cf-PWV</td>
<td>10.8±2.2</td>
<td>Sphygmocor device</td>
</tr>
<tr>
<td>Durmus, I. 2014[15]</td>
<td>38</td>
<td>Turkey</td>
<td>AAA:69±4</td>
<td>11(61%)</td>
<td>26.7±4.4</td>
<td>18/20</td>
<td>cf-PWV</td>
<td>14.8±4.9</td>
<td>Sphygmocor device</td>
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<td>Bailey, M. A. 2014[16]</td>
<td>309</td>
<td>UK</td>
<td>AAA:73±7.5</td>
<td>120(74.5%)</td>
<td>28±4.6</td>
<td>148/161</td>
<td>cf-PWV</td>
<td>9.55±2.3</td>
<td>Vicoder device</td>
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<tr>
<td>Li, R. X. 2013[24]</td>
<td>20</td>
<td>USA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>5/15</td>
<td>Aortic PWV</td>
<td>10.54±6.52</td>
<td>A Sonix RP system</td>
</tr>
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<td>Lee, C. W. 2013[20]</td>
<td>102</td>
<td>Taiwan</td>
<td>AAA:75.2±11.6</td>
<td>47(92.2%)</td>
<td>23.8±4.2</td>
<td>51/51</td>
<td>cf-PWV</td>
<td>12.1±2.7</td>
<td>Colin VP-200</td>
</tr>
<tr>
<td>Kadoglou, N. P. E. 2012[22]</td>
<td>79</td>
<td>Greece</td>
<td>AAA:71±4</td>
<td>48(100%)</td>
<td>28.6±4.2</td>
<td>48/31</td>
<td>cf-PWV</td>
<td>13.11±3.57</td>
<td>Complior SP, Alam Medical,France</td>
</tr>
<tr>
<td>Li, R. X. 2011[23]</td>
<td>10</td>
<td>USA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>2/8</td>
<td>Aortic PWV</td>
<td>10.54±6.52</td>
<td>A Sonix RP system</td>
</tr>
<tr>
<td>Li L2016[14]</td>
<td>26</td>
<td>China</td>
<td>NA</td>
<td>10(76.9%)</td>
<td>NA</td>
<td>13/13</td>
<td>Aortic PWV</td>
<td>18.63±1.3</td>
<td>Electrocardiographic Gated 64-Detector CT</td>
</tr>
</tbody>
</table>

NA: not available

*PWV(Pulse wave velocity)

*AAA(abdominal aortic aneurysm)

*cf-PWV(carotid-femoral PWV, cfPWV)

*Aortic PWV (the infrarenal PWV)

**Table 2:** Subgroup analysis of PWV in AAA group and control group
<table>
<thead>
<tr>
<th>Subgroup</th>
<th>N</th>
<th>WMD(95%CI)</th>
<th>Test of SMD=0</th>
<th>Heterogeneity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Z P for Z</td>
<td>$\chi^2$ (%)</td>
</tr>
<tr>
<td><strong>All studies</strong></td>
<td>9</td>
<td>2.23(2.02,2.70)</td>
<td>98.9</td>
<td>0.000</td>
</tr>
<tr>
<td><strong>Age between AAA and control</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Significance difference</td>
<td>4</td>
<td>-0.48(-0.94,0.01)</td>
<td>2.01 0.044</td>
<td>77.0 0.005</td>
</tr>
<tr>
<td>Not significance difference</td>
<td>5</td>
<td>5.59(5.09,6.09)</td>
<td>22.04 0.000</td>
<td>99.0 0.000</td>
</tr>
<tr>
<td><strong>Diabetes between AAA and control</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Significance difference</td>
<td>1</td>
<td>-2.10(-3.23,-0.97)</td>
<td>3.63 0.000</td>
<td>/</td>
</tr>
<tr>
<td>Not significance difference</td>
<td>4</td>
<td>0.52(0.11,0.93)</td>
<td>2.49 0.013</td>
<td>95.2 0.000</td>
</tr>
<tr>
<td><strong>Hypertension between AAA and control</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Significance difference</td>
<td>2</td>
<td>-0.52(--0.99,-0.06)</td>
<td>2.20 0.028</td>
<td>88.8 0.003</td>
</tr>
<tr>
<td>Not significance difference</td>
<td>3</td>
<td>2.05(1.23,2.87)</td>
<td>4.89 0.000</td>
<td>96.7 0.000</td>
</tr>
<tr>
<td><strong>Sex between AAA and control</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Significance difference</td>
<td>1</td>
<td>-0.2(-0.71,0.31)</td>
<td>0.76 0.445</td>
<td>/</td>
</tr>
<tr>
<td>Not significance difference</td>
<td>6</td>
<td>4.35(3.89,4.80)</td>
<td>18.73 0.000</td>
<td>99.1 0.000</td>
</tr>
<tr>
<td><strong>Smoking between AAA and control</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Significance difference</td>
<td>2</td>
<td>1.12(0.44,1.81)</td>
<td>3.23 0.001</td>
<td>98.0 0.000</td>
</tr>
<tr>
<td>Not significance difference</td>
<td>4</td>
<td>0.43(-0.00,0.87)</td>
<td>1.94 0.052</td>
<td>96.3 0.000</td>
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<tr>
<td><strong>Detection location</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>cf-PWV</td>
<td>6</td>
<td>0.63(0.26,1.00)</td>
<td>3.37 0.001</td>
<td>96.2 0.000</td>
</tr>
<tr>
<td>Aortic PWV</td>
<td>3</td>
<td>2.36(2.02,2.70)</td>
<td>27.65 0.000</td>
<td>81.9 0.004</td>
</tr>
</tbody>
</table>

*AAA(abdominal aortic aneurysm)*

**Figures**
Records identified through database searching (n=244): PubMed (171); Embase (68); CINII (5).

244 of records collected → 103 duplicated articles excluded

141 of records screened → 123 of records excluded

18 of full-text articles assessed for eligibility

3 not about PWV and abdominal aortic aneurysm
1 data can’t be extracted
1 data can’t be extracted
2 Review articles
2 Not found the full text
1 animal study

9 of studies included in qualitative synthesis and meta-analysis

Figure 1
Flow diagram of the literature.

(A) Forest plot comparing PWV levels between AAA patients and non-AAA control. (B) Funnel plot of the association between PWV and AAA.
Figure 3

Forest plots of meta-analysis data (A) subgroup analysis according to significant difference or not significant difference in age between AAA and control group; (B) subgroup analysis according to PWV measurement location (carotid-femoral PWV and aortic PWV).

Figure 4

Forest plots of meta-analysis data (A) subgroup analysis according to significant difference or not significant difference in hypertensive between AAA and control group; (B) subgroup analysis according to significant difference or not significant difference in diabetes between AAA and control group.
Figure 5

Forest plots of meta-analysis data (A) subgroup analysis according to significant difference or not significant difference in sex between AAA and control group; (B) subgroup analysis according to significant difference or not significant difference in smoking between AAA and control group.