Journal of the American Heart Association

SYSTEMATIC REVIEW AND META-ANALYSIS

Systematic Review and Meta-Analysis of Peak Wall Stress and Peak Wall Rupture Index in Ruptured and Asymptomatic Intact Abdominal Aortic Aneurysms

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BACKGROUND: Prior studies have suggested aortic peak wall stress (PWS) and peak wall rupture index (PWRI) can estimate the rupture risk of an abdominal aortic aneurysm (AAA), but whether these measurements have independent predictive ability over assessing AAA diameter alone is unclear. The aim of this systematic review was to compare PWS and PWRI in participants with ruptured and asymptomatic intact AAAs of similar diameter.

METHODS AND RESULTS: Web of Science, Scopus, Medline, and The Cochrane Library were systematically searched to identify studies assessing PWS and PWRI in ruptured and asymptomatic intact AAAs of similar diameter. Random-effects meta-analyses were performed using inverse variance-weighted methods. Leave-one-out sensitivity analyses were conducted to assess the robustness of findings. Risk of bias was assessed using a modification of the Newcastle-Ottawa scale and standard quality assessment criteria for evaluating primary research papers. Seven case-control studies involving 309 participants were included. Meta-analyses suggested that PWRI (standardized mean difference, 0.42; 95% CI, 0.14–0.70; P=0.004) but not PWS (standardized mean difference, 0.13; 95% CI, −0.18 to 0.44; P=0.418) was greater in ruptured than intact AAAs. Sensitivity analyses suggested that the findings were not dependent on the inclusion of any single study. The included studies were assessed to have a medium to high risk of bias.

CONCLUSIONS: Based on limited evidence, this study suggested that PWRI, but not PWS, is greater in ruptured than asymptomatic intact AAAs of similar maximum aortic diameter.

Key Words: abdominal aortic aneurysm ■ biomechanics ■ computed tomography ■ finite element analysis ■ imaging ■ meta-analysis ■ systematic review

Abdominal aortic aneurysm (AAA) rupture is estimated to be responsible for 200 000 deaths annually worldwide.[1,2] AAA rupture is thought to occur when the hemodynamic forces exceed the aortic wall strength.[1,3] In clinical practice, maximum AAA diameter is the main measure used to estimate rupture risk and select patients for elective repair.[1] Current guidelines recommend elective repair of asymptomatic large AAAs (maximum aortic diameter ≥50 mm in women and ≥55 mm in men).[1,4,5] Approximately 1% to 2% of small asymptomatic AAAs rupture each year[4] and some large AAAs remain stable during a patient's lifetime,[6] suggesting that diameter is an imperfect measure of rupture risk.

Biomechanical imaging may provide a more precise means to estimate AAA rupture risk and select patients for repair. Finite element analysis (FEA) can noninvasively estimate the maximum tensile stress

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Supplementary Material for this article is available at https://www.ahajournals.org/doi/suppl/10.1161/JAHA.120.019772

For Sources of Funding and Disclosures, see page 10.

JAHA is available at: www.ahajournals.org/journal/jaha

CLINICAL PERSPECTIVE

What Is New?

- Prior studies have suggested that aortic peak wall stress and peak wall rupture index can predict abdominal aortic aneurysm rupture. However, the value of measuring peak wall stress and peak wall rupture index over simply measuring maximum abdominal aortic aneurysm diameter is unclear.
- This systematic review and meta-analysis suggests that peak wall rupture index, but not peak wall stress, is greater in ruptured than asymptomatic intact abdominal aortic aneurysms of similar diameter.

What Are the Clinical Implications?

- The measurement of peak wall rupture index may add to that of maximum aortic diameter in assessing the risk of abdominal aortic aneurysm rupture.

Nonstandard Abbreviations and Acronyms

FEA	finite element analysis
PWRI	peak wall rupture index
PWS	peak wall stress
SMD	standardized mean differences

within the AAA wall (peak wall stress; PWS) and the maximum ratio between wall stress and the estimated local wall strength (peak wall rupture index; PWRI).[3] Semiautomated systems have been developed to enable clinicians without engineering backgrounds to perform FEA using computed tomography (CT) scans that are routinely performed to assess people with AAA (Figure 1).[3,7] Thus, it would be feasible to use PWS and/or PWRI in clinical practice if these measures were shown to be independent predictors of AAA rupture. Currently, however, the value of measuring PWS and PWRI over simply measuring maximum AAA diameter is unclear.

Previous meta-analyses[3,8] have suggested that PWS is greater in patients with ruptured than intact AAAs; however, the generalizability of this finding is unclear owing to a number of limitations. These included lack of adjustment or matching for aortic diameter,[3] inclusion of symptomatic AAAs mixed with ruptured AAAs,[8] and small sample sizes.[9] These limitations have been addressed in more recent studies that have been reported after the publication of the most recent meta-analysis,[7,8] suggesting that higher quality data are now available for an updated meta-analysis. Furthermore, PWRI has been suggested by one,[10] but not another study,[11] to be a superior measure of rupture risk than PWS. No meta-analysis comparing PWRI in ruptured and intact AAA has been reported.[3,8] The aim of this systematic review and meta-analysis was to provide an up-to-date pooled analysis of prior studies that compared PWS and PWRI in patients with ruptured and asymptomatic intact AAA of similar diameter.

METHODS

Literature Search and Inclusion Criteria

The data that support the findings of this study are available from the corresponding author upon reasonable request. This systematic review and meta-analysis was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement.[12] A study protocol for this systematic review was designed (Data S1) and was not preregistered with any database. A literature search was performed using the following databases: Web of Science (via Institute for Scientific Information Web of Knowledge; 1965), Scopus (1966), Medline (via OvidSP, 1966), and The Cochrane Library to identify case-control studies investigating PWS in patients with ruptured and diameter matched asymptomatic intact AAAs. The following search terms were applied: “peak wall stress” OR “peak wall rupture index” OR “rupture potential index” AND “abdominal aortic aneurysm.” The search was performed in October 2020 without language restrictions by one author (T.P.S.). Reference lists of primary articles and reviews were searched to increase the yield of relevant publications. Titles and abstracts were screened to identify relevant studies. If the suitability of an article was uncertain, the full text was reviewed. For inclusion in the meta-analysis studies needed to have compared PWS or PWRI in asymptomatic intact AAAs and ruptured AAAs of similar diameter (within 3 mm mean difference between groups). Studies in which it was not possible to separate symptomatic from ruptured AAAs were excluded.

Data Extraction and Risk of Bias of the Included Studies

Data were extracted from included studies independently by 3 authors (T.S., J.M., and J.G.). The following data were collected: sample sizes for the ruptured and intact AAA group; study design; software used to perform FEA, PWS, and PWRI estimates; AAA diameter; risk factors (including age, sex, smoking history, hypertension, diabetes mellitus, ischemic heart disease;

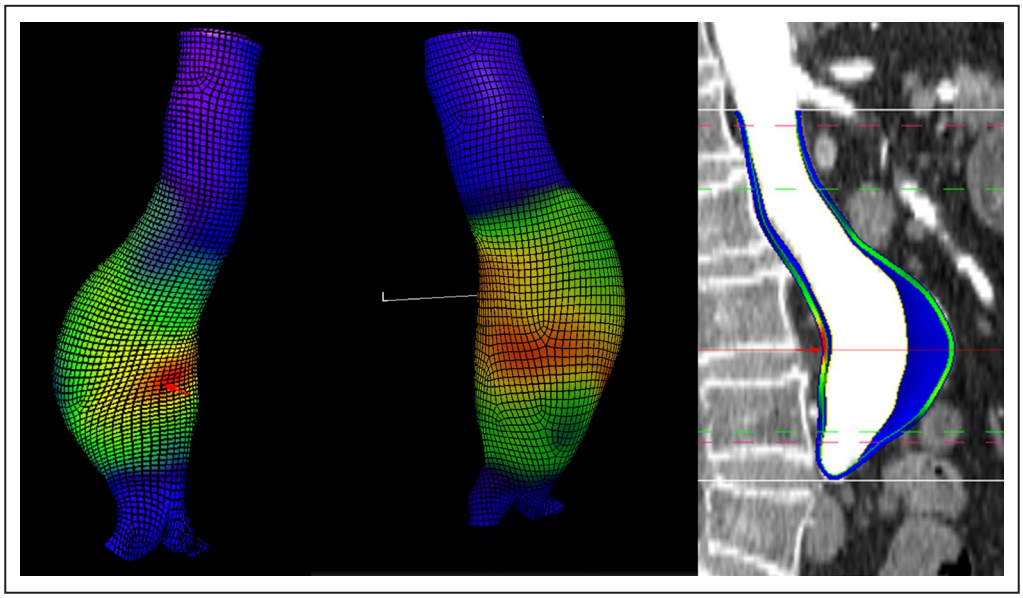

Figure 1. Examples of 3-dimensional segmentation produced using finite element analysis from computed tomography images of patients with AAA.
The red areas indicate areas of high aortic wall stress. AAA indicates abdominal aortic aneurysm.

stroke; chronic obstructive pulmonary disease); and systolic blood pressure. If relevant data were not reported in the publication, the corresponding author was contacted for this information. The risk of bias was assessed independently by 3 authors (T.S., J.M., and J.G.). A quality assessment tool was designed to assess the risk of bias of the included studies adapted from 2 previously reported tools (Newcastle-Ottawa scale and Standard Quality Assessment Criteria for Evaluating Primary Research Papers).[13,14] A number of additional aspects of the included studies relevant to this systematic review were also assessed including criteria used to define AAA rupture, method used to estimate PWS and PWRI and reproducibility reported, use of a standardized blood pressure in PWS and PWRI calculations (ie, use of a single blood pressure measurement for all participants or omission of blood pressure in calculations), inclusion of CT scan before or after rupture (for ruptured cases), matching for AAA diameter between asymptomatic intact and ruptured cases, and matching for other confounding variables. The overall risk of bias assessed within each study was assessed as low, medium, or high based on predefined criteria. Details regarding the quality assessment criteria can be found in Table S1.

Statistical Analysis

Meta-analysis was performed using inverse variance-weighted methods[15] in order to calculate standardized mean differences (SMD) with 95% (CI. PWS outcome data were converted from newton per square centimeter (N/cm^2) to kilopascal (kPa) where required.[16] Because of anticipated interstudy heterogeneity in methods and biomechanical analyses, SMDs were calculated using random-effects models.[17] Interstudy heterogeneity was assessed using the I^2 index and values <25%, between 25% to 75%, and >75% were considered to represent low, moderate, and high heterogeneity, respectively.[18] If PWS and PWRI were computed at a standardized blood pressure (ie, same blood pressure for all participants) this value was used in the meta-analysis. One study calculated PWS and PWRI using a standardized blood pressure of 140/80 mm Hg for the main analysis and sensitivity analyses were performed using a lower (120/70 mm Hg) and higher (160/90 mm Hg) blood pressure.[7] For that study, results from the main analysis were used in the meta-analysis. If studies did not use a standardized blood pressure, PWS and PWRI values computed with patient-specific blood pressures were used.[11,19,20] In one study the SD of PWS was not reported and this was derived from the SE using Review Manager version 5.4 (The Cochrane Collaboration) as previously described.[3,17] To identify sources of heterogeneity a leave-one-out-sensitivity analysis was performed by excluding individual studies one at a time and recalculating the pooled estimates for the remaining studies. Publication bias was assessed by funnel plots comparing the summary estimate of each study to its precision (1/SE) for outcomes that were reported in ≥5 studies.[21] Analyses were conducted using Stata version 16.1 (StataCorp LP, College Station, TX). All statistical tests were 2-sided and a P value of <0.05 was considered significant.

RESULTS

Study Identification

The initial database searches identified 836 studies after removal of duplicates. After title and abstract screening, the full texts of 20 studies were assessed against the inclusion criteria. Thirteen articles were excluded after full text review. Common reasons for exclusion included mismatch in AAA diameter between ruptured and intact AAAs,[22] inclusion of symptomatic but not ruptured AAAs[22–24] and lack of comparison of PWS or PWRI between ruptured and intact AAAs.[25] Ultimately 7 studies were included (Figure 2).

Study Characteristics

A total of 309 participants with ruptured (n=139) and asymptomatic intact (n=170) AAAs of similar aortic diameter were investigated in the 7 included studies.[7,10,11,16,19,20,26] All studies were of case-control design and sample sizes ranged between 14 and 75 (see Table 1).[7,10,11,16,19,20,26] Three studies were performed in Sweden[10,19,26] and the remaining studies were conducted in Australia,[7] Spain,[11] Czechia,[20] and The Netherlands.[16] Six studies used the A4 Clinics 5.0 (VASCOPS GmbH, Graz, Austria) platform[7,10,11,19,20,26] and 1 study used ABAQUS v.6.5 (Hibbit, Karlsson and Sorensen, Inc, Pawtucket, RI) for FEA.[16] One study used a combination of the A4 Clinics 5.0 and the ANSYS (Ansys Inc.) platforms.[20] The inclusion criteria varied between studies. In 4 studies AAA cases were included only if the available CT scan satisfied specific imaging criteria,[7,11,19,26] whereas other studies did not report this as a requirement for inclusion.[10,16,20] The imaging criteria used to select CT scans differed between studies. One study specifically reported excluding patients with juxtarenal or thoracoabdominal aneurysms and patients with ruptured AAAs that had massive contrast extravasation.[7] Another study included only participants

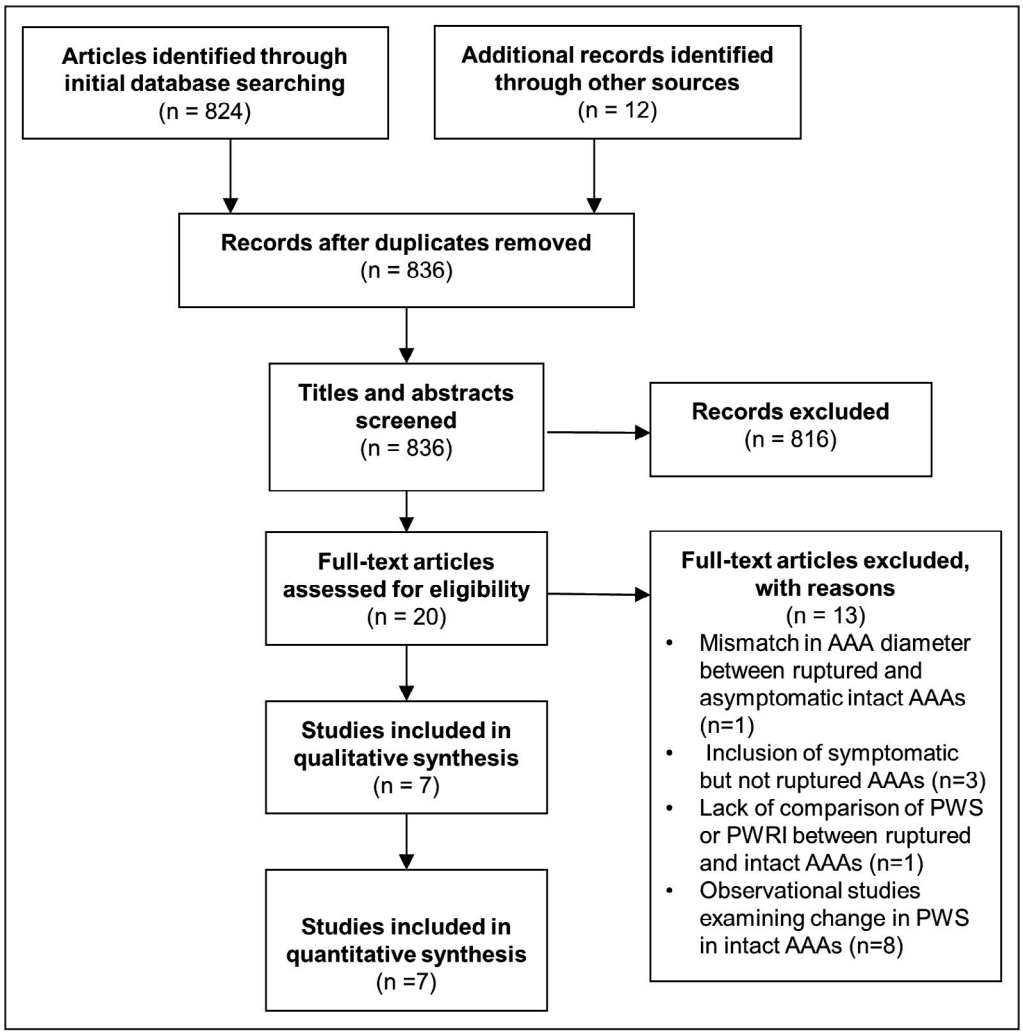

Figure 2. PRISMA diagram describing the literature search.
AAA indicates abdominal aortic aneurysm; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; PWRI, peak wall rupture index; and PWS, peak wall stress.

Table 1. Characteristics of Case Control Studies Comparing PWS and PWRI Between Ruptured and Asymptomatic Intact AAAs of Similar Aortic Diameter

Study	Total Sample Size	Sample Size (Asymptomatic Intact: Ruptured)*	Biomechanical Measurements	Software Used	Variables That Were Balanced Between Asymptomatic iAAA and rAAAs	Blood Pressure Used in PWS or PWRI Analysis	Reproducibility of Biomechanical Measurements
Singh et al (2020)[7]	75	75 (50:25)	PWS, PWRI	A4 Clinics 5.0 (VASCOPS GmbH, Graz, Austria).	Diameter and blood pressure	Standardized blood pressure (140/80 mm Hg) used and sensitivity analysis with lower and higher blood pressures (120/70 mm Hg and 160/90 mm Hg) for all participants	Intraobserver reproducibility; CV 2.7% and 4.7% for PWS in iAAA and rAAAs respectively
Siika et al (2019)[10]	283	60 (40:20)	PWS, PWRI	A4 Clinics 5.0 (VASCOPS GmbH, Graz, Austria)	Diameter, sex, age and blood pressure	Blood pressure omitted from analyses	NR
Siika et al (2018)[19]	90	43 (15:28)	PWS, PWRI	A4 Clinics 5.0 (VASCOPS GmbH, Graz, Austria)	Diameter	Patient-specific blood pressure; timing of blood pressure measurement in relation to CT scan not reported	Intraobserver reproducibility; Mean % difference of 6.86±6.46 and 7.70±6.26 for PWS and PWRI respectively. Interobserver reproducibility; mean % difference 7.09±6.16 and 9.47±8.18†
Leemans et al (2018)[11]	175	62 (31:31)	PWS, PWRI, rupture risk equivalent diameter	A4 Clinics 5.0 (VASCOPS GmbH, Graz, Austria).	Diameter	Patient-specific blood pressure obtained from the last measurement in a noncritical setting within 1 year before presentation	NR
Polzer et al (2015)[20]	14	14 (7:7)	PWRI and probabilistic rupture risk index	A4 Clinics 5.0 (VASCOPS GmbH, Graz, Austria) and ANSYS (Ansys Inc.)	Diameter	Patient-specific blood pressure; timing of blood pressure measurement not reported	Intraobserver reproducibility; CV <5.5% for PWS and PWRI in participants with iAAAs. Interobserver reproducibility; intraclass correlation coefficient 0.98 (range 0.97–0.99) for PWS and PWRI†
Gasser et al (2010)[26]	50	35 (17:18)	PWS, PWRI	A4 Clinics 5.0 (VASCOPS GmbH, Graz, Austria)	Diameter and blood pressure	Participants were matched for blood pressure between groups. Blood pressure measurements obtained in the same admission in which CT scan was performed or earlier hospital or healthcare center visit (for ruptured cases)	NR
Truijers et al (2007)[16]	30	20 (10:10)	PWS	ABAQUS v.6.5 (Hibbit, Karlsson and Sorensen, Inc, Pawtucket, RI)	Diameter and blood pressure	Patient-specific blood pressure obtained from a year before CT scan; Sensitivity analysis also performed in which a standardized blood pressure (120 mm Hg systolic) was used	NR

AAA indicates abdominal aortic aneurysm; CT, computed tomography; CV, coefficient of variation; iAAA, asymptomatic intact AAA; NR, not reported; PWRI, peak wall rupture index; PWS, peak wall stress; and rAAA, ruptured AAA.

*Sample sizes reported are reflective of the cases and control that were similar in AAA diameter and excluded symptomatic AAA cases.

†Reported in an external publication.

with CT scans in which the aorta was visible from the renal arteries to the iliac bifurcation and the lumen was distinguishable from intraluminal thrombus.[11] One study required CT scans to have a sufficiently high out-of-plane image resolution with good visibility of the exterior aneurysm surface.[26] In another study, only participants with good quality CT scans were included; however, the criteria used to determine this were not reported.[19] All studies either matched cases and controls for aortic diameter or included cases and controls with similar mean aortic diameter (within 3 mm difference; see Tables 1 and 2). Three studies used a standardized blood pressure to compute PWS or PWRI in all participants,[7] or matched cases and controls for blood pressures,[26] or omitted blood pressure from calculations.[10] The remaining studies used patient-specific blood pressures although the relationship between their measurement and the timing of CT scan varied across studies (Table 1). For ruptured AAA cases, blood pressure readings before rupture were frequently used.[11,16,26] For participants with asymptomatic intact AAAs, measurements were either taken from the same hospital visit[26] in which the CT scan was performed or from a prior visit.[11,16] The timing of blood pressure measurements in relation to CT scans were not reported in 2 studies.[19,20] Three studies reported the reproducibility of their FEA estimates (Table 1).[7,19,20]

Participant Characteristics

The participant characteristics are summarized in Table 2. The average age of participants ranged between 70 and 79 years.[7,10,16,19,26] There were no significant differences in the average age of participants between asymptomatic intact and ruptured AAA groups in the 3 studies that statistically assessed this.[7,10,19] The proportions of men in the asymptomatic intact and ruptured groups were 60% to 94% and 55% to 78% respectively. One study included a significantly larger proportion of women in the ruptured AAA group,[7] whereas 2 studies reported no significant differences in sex between groups.[10,19] The remaining studies either did not report sex[11,20] or did not statistically compare this.[16,26] Details regarding diabetes mellitus, ischemic heart disease, stroke, chronic obstructive pulmonary disease, smoking, and blood pressure were reported in only 2 studies (Table 2).

Risk of Bias Assessment

The methodological quality assessment and overall risk of bias of the included studies are reported in Figure 3. Six studies were assessed to have a high risk of bias,[10,11,16,19,20,26] and 1 study was assessed to have a medium risk of bias.[7] Six studies were of retrospective design, and the design of 1 study was unclear.[20] Only 1 study used an objective definition of AAA rupture, which was defined as the presence of blood in the retroperitoneum or peritoneum identified on CT by a consultant vascular specialist.[7] The method of estimating PWS and PWRI was well described in 3 out of the 7 studies that included the reporting of the reproducibility of the method[7] within the same or a previous publication (see Figure 3).[19,20] Only 2 of these studies assessed intra- and interobserver reproducibility (see Table 1).[19,20] One study assessed the reproducibility of methods in both asymptomatic and ruptured AAAs (coefficients of variation 2.7% and 4.7% for PWS in asymptomatic intact AAA and ruptured AAAs respectively[7]), whereas in the other 2 studies reproducibility was assessed in asymptomatic intact AAAs only. Six studies matched ruptured and asymptomatic intact AAA cases by AAA diameter,[7,10,11,19,20,26] whereas in one study participants were not matched; however, the mean diameter between intact and ruptured cases was similar (51±2 versus 53±2 mm respectively).[16] Three studies used a standardized blood pressure to calculate PWS and PWRI whereas the other 3 studies[11,19,20] used patient-specific blood pressures. One study matched participants for age and sex[10] in addition to AAA diameter. An a priori sample size calculation was performed in only 1 study.[7]

Reported Association of PWS and PWRI With AAA Rupture

The mean aortic diameter of included patients ranged between 51 to 82 mm and 53 to 82 mm in included asymptomatic intact and ruptured AAAs respectively (see Table 3). No significant differences in PWS between groups were reported, although in one study PWS was not assessed[20] and another study did not statistically compare PWS between groups in the matched participants.[26] PWRI was significantly higher in ruptured AAAs than asymptomatic intact AAAs in 2 studies.[10,19] PWRI was higher in the remaining studies that assessed this[7]; however, differences were not statistically significant (see Table 3).[7,11]

Data Synthesis

In the meta-analysis, PWS was not significantly different between ruptured and asymptomatic AAAs (SMD, 0.13; 95% CI, −0.18 to 0.44; P=0.418; Figure 4). Moderate heterogeneity was observed (I^2=40.6%). In contrast, PWRI was significantly higher in participants with ruptured compared with asymptomatic intact AAA (SMD, 0.42; 95% CI, 0.14–0.70, P=0.004; Figure 5). Interstudy heterogeneity was low (I^2=25.5%). Leave-one-out sensitivity analysis suggested that the results of the meta-analyses were not dependent on the inclusion of any single study (Figures S1 and S2). The funnel plot for PWRI appeared asymmetrical (Figure S3) suggesting potential publication bias.

Table 2. Clinical Characteristics of Participants With Ruptured and Asymptomatic Intact AAAs of Similar Aortic Diameter

Study	Group	Number	Age, y	Male	Diabetes Mellitus	Ischemic Heart Disease	Stroke	Chronic Obstructive Pulmonary Disease	Smoking	Systolic Blood Pressure (mm Hg)
Singh et al (2020)[7]	iAAA	50	72±7	94	18	52	10	24	94	140*
	rAAA	25	73±7	72	13	38	0	13	88	140*
Siika et al (2019)[10]	iAAA	40	78±7	60	NR	NR	NR	NR	NR	NR†
	rAAA	20	79±7	55	NR	NR	NR	NR	NR	NR†
Siika et al (2018)[19]	iAAA	15	75±8	87	NR	NR	NR	NR	NR	NR
	rAAA	28	76±10	75	NR	NR	NR	NR	NR	NR
Leemans et al (2018)[11]	iAAA	31	NR	NR	NR	NR	NR	NR	NR	NR
	rAAA	31	NR	NR	NR	NR	NR	NR	NR	NR
Polzer et al (2015)[20]	iAAA	7	NR	NR	NR	NR	NR	NR	NR	132±8
	rAAA	7	NR	NR	NR	NR	NR	NR	NR	152±26
Gasser et al (2010)[26]	iAAA	17	75±8	78	NR	NR	NR	NR	NR	NR‡
	rAAA	18	76±11	78	NR	NR	NR	NR	NR	NR‡
Truijers et al (2007)[16]	iAAA	10	72±2	90	10	70	20	30	40	120*
	rAAA	10	70±2	70	10	30	20	20	40	120*

Values are expressed as mean±SD, median [interquartile range] or n (%). AAA indicates abdominal aortic aneurysm; iAAA, asymptomatic intact AAA; NR, not reported; and rAAA, ruptured AAA.
*A standardized blood pressure was used for biomechanical analyses.
†Blood pressure was omitted from patient-specific parameters.
‡iAAAs and rAAAs were matched for blood pressure.

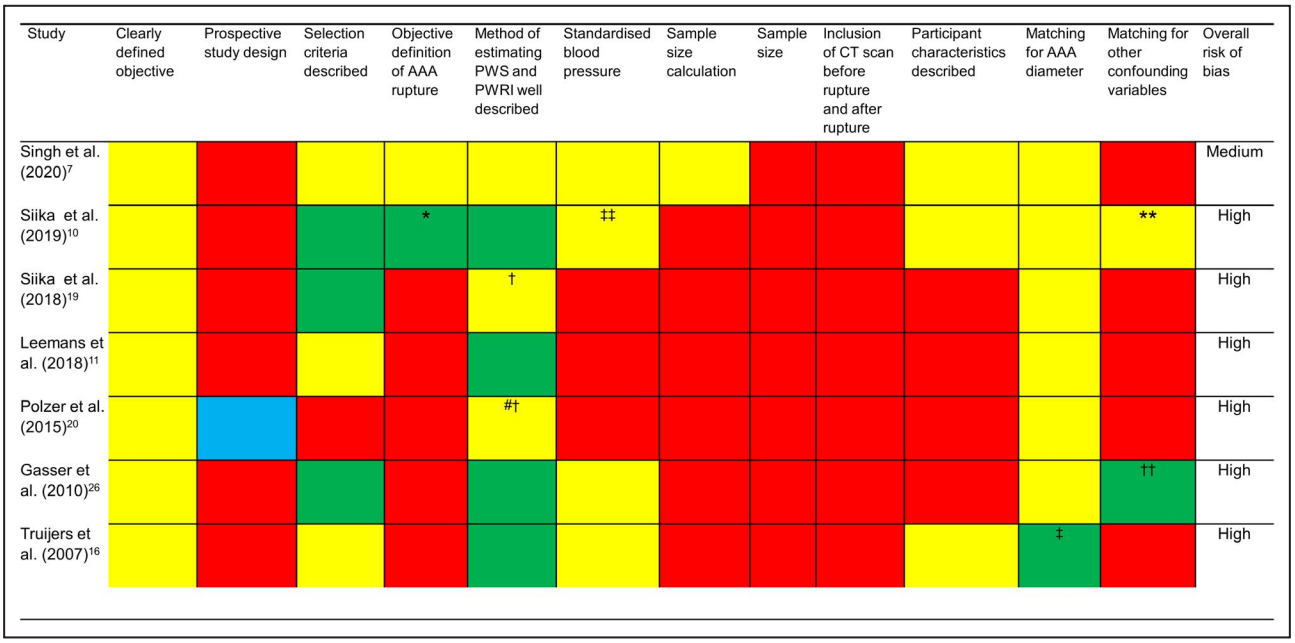

Figure 3. Strengths and weaknesses of studies included in this systematic review.
The yellow and red colored cells represent criteria, which were and not met in each study respectively. For the sample size criterion, red colored cells represent studies that had a sample size <100 and yellow-colored cells represent studies that had sample sizes >100. The green colored cells represent criteria that were partially met in each study. A blue colored cell was used if it was unclear whether a criterion was met by a study. AAA indicates abdominal aortic aneurysm; CT, computed tomography; PWRI, peak wall rupture index; and PWS, peak wall stress. *AAA rupture cases were identified using an International Classification; **cases and controls matched for age and sex; †reproducibility reported in an external publication; ††cases and controls matched for blood pressure; ‡cases and controls were not matched by study design although AAA diameter was similar between groups; ‡‡in this study blood pressure was omitted from biomechanical calculations; #PWS not assessed in this study.

DISCUSSION

This meta-analysis suggested that PWRI, but not PWS, is greater in ruptured than asymptomatic intact AAAs of similar diameter. This finding is in contrast with a previous meta-analysis that reported greater PWS in ruptured than intact AAAs.[3] A major limitation of the previous meta-analysis was the mismatch

Table 3. Comparison of PWS and PWRI of Participants With Ruptured and Asymptomatic Intact AAAs of Similar Aortic Diameter

Study	Group	Number	Diameter (mm)	*P* Value	PWS (kPa)	*P* Value	PWRI	*P* Value
Singh et al (2020)[7]	iAAA	50	82±14	0.906	263.8±69.4	0.192	1.09±0.52	0.982
	rAAA	25	82±13		279.8±90.5		1.20±0.76	
Siika et al (2019)[10]	iAAA	40	53±5	0.319	197.0±40.3	0.162	0.35±0.08	0.016
	rAAA	20	55±5		216.3±45.3		0.43±0.11	
Siika et al (2018)[19]	iAAA	15	73±11	0.674	284±53.4*	0.194	0.48±0.11*	<0.001
	rAAA	28	74±12		249±53.9*		0.80±0.54*	
Leemans et al (2018)[11]	iAAA	31	71±15	0.81	261±89†	0.99	0.69±0.33	0.61
	rAAA	31	72±18		262±75†		0.70±0.27	
Polzer et al (2015)[20]	iAAA	7	73±11	NR	NR		0.48±0.41‡	NR
	rAAA	7	76±14		NR		0.69±0.41‡	
Gasser et al (2010)[26]	iAAA	17	75±12	NR	292.0±108.7	NR	0.61±0.26	NR
	rAAA	18	77±15		330.8±114.2		0.74±0.29	
Truijers et al (2007)[16]	iAAA	10	51±2	0.57	317±73†	0.30	NR	
	rAAA	10	53±2		367±126†		NR	

Values are expressed as mean±SD unless indicated otherwise. AAA indicates abdominal aortic aneurysm; iAAA, asymptomatic intact AAA; kPa, kilopascal; NR, not reported; PWRI, peak wall rupture index; PWS, peak wall stress; and rAAA, ruptured AAA.

*SDs not available and were imputed from the diameter mismatched analysis reported in the same study.

†PWS converted from newton per square centimeter to kPa.

‡Derived PWRI values reported that have been divided by the mean arterial pressure inflation factor used in the study to obtain comparable results.

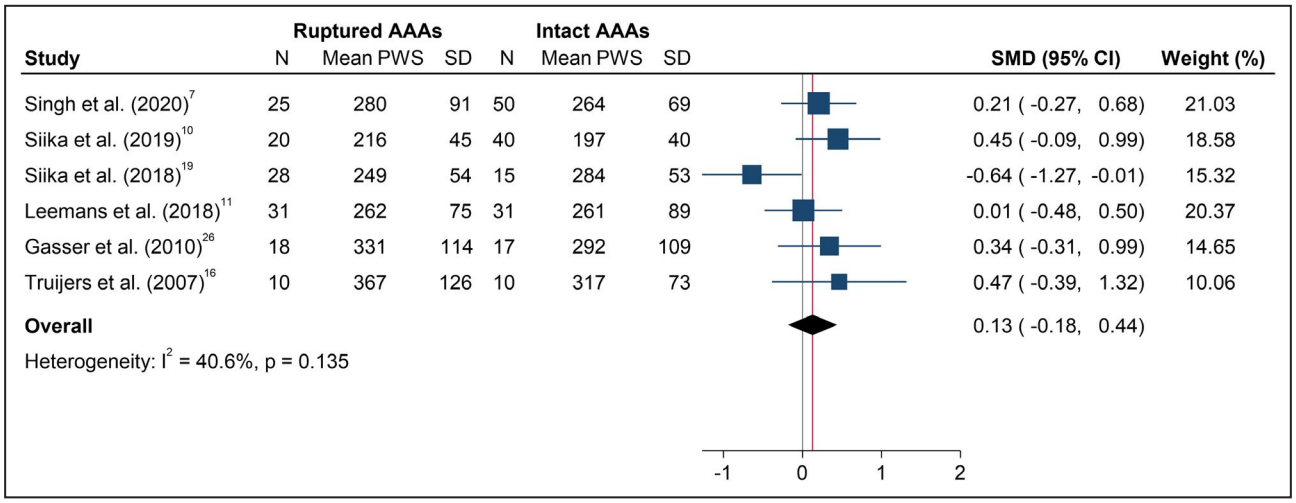

Figure 4. Differences in peak wall stress in ruptured and asymptomatic intact AAAs.
The SMD is the mean difference between both groups, standardized to 1 SD difference in PWS (kilopascal) within that study. The summary SMD is estimated from inverse variance-weighted meta-analysis. Box areas are inversely proportional to the variance of the SMD and horizontal lines illustrate 95%CIs. AAA indicates abdominal aortic aneurysm; PWS, peak wall stress; and SMD, standardized mean difference.

in aortic diameter between groups and inclusion of symptomatic patients in the ruptured group. Participants with symptomatic intact AAAs were not included in the current study as their risk of rupture is uncertain.[5,9]

Maximum aortic diameter is currently the most established measure of AAA rupture risk.[1,5,27] There are, however, a number of limitations in using aortic diameter in clinical practice, in particular the measurement error, which may be greater than the annual change in diameter.[28,29] Additional methods of estimating rupture risk and determining management may therefore be valuable. The findings of this study suggest that measurement of PWRI may add to aortic diameter in assessing the risk of AAA rupture. There are, however, many limitations of this technology that need to be addressed. There is currently no standardized approach to conducting FEA. There was substantial variation in the approach used to incorporate blood pressures in the calculation of PWS and PWRI in the included studies. Some studies used an arbitrary blood pressure for all participants, whereas others used patient-specific blood pressures. It is currently unclear which approach is most appropriate. Additionally, wall thickness and strength have an

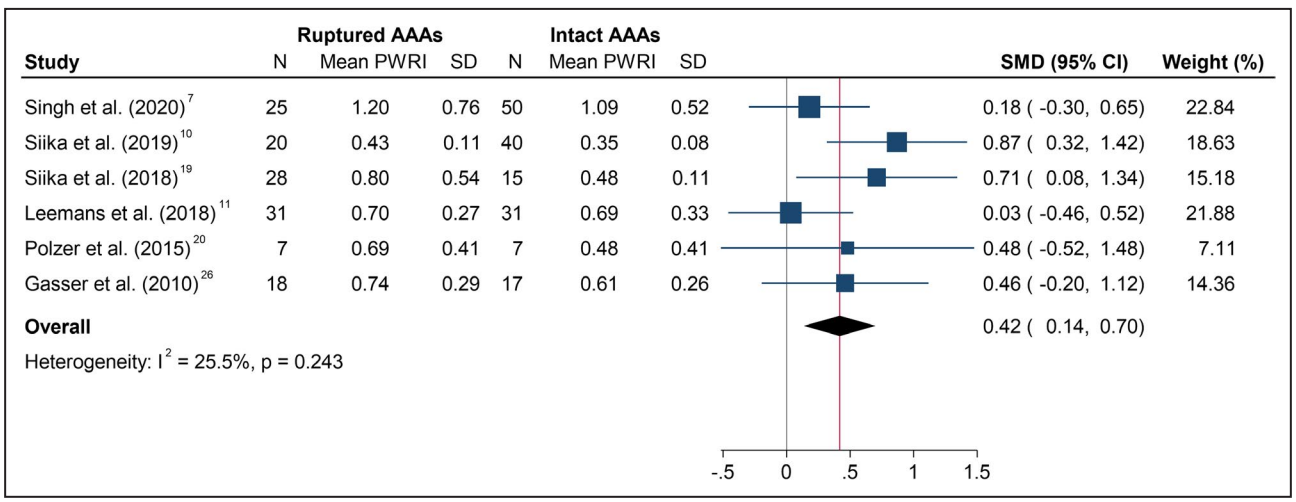

Figure 5. Differences in peak wall rupture index in ruptured and asymptomatic intact AAAs.
The SMD is the mean difference between both groups, standardized to 1 SD difference in PWRI within that study. The summary SMD is estimated from inverse variance-weighted meta-analysis. Box areas are inversely proportional to the variance of the SMD and horizontal lines illustrate 95% CIs. AAA indicates abdominal aortic aneurysm; CT, computed tomography; PWRI, peak wall rupture index; and SMD, standardized mean difference.

important effect on the risk of aortic rupture and prior investigations have suggested that increased aortic wall thickness is associated with reduced aortic wall stress.[26,30] Currently there is no accurate and feasible method to estimate wall thickness from imaging.[7] Six of the 7 studies used FEA software to estimate PWRI using the same formula that was derived from prior tensile testing of human AAA wall specimens ex vivo, but this may not be representative of the situation in individual patients in vivo.[30] Aortic calcification has previously been suggested to have an important influence on biomechanical forces but there remains no standardized method of including this in estimations of wall stress.[31,32]

Although the current meta-analysis suggested that PWRI is likely to be higher in ruptured AAAs compared with asymptomatic intact AAAs of similar diameter, the confidence in this finding is lessened as the included studies were assessed to have either a medium or high risk of bias because of a number of design limitations. First, studies included participants with CT scans performed after rupture and it is likely that the biomechanical forces before rupture were different. Second, some studies used patient-specific blood pressures to perform biomechanical analyses rather than a standardized blood pressure.[11,19,20] This may have contributed to heterogeneity and led to under- or overestimation of PWS and PWRI. Although patients with asymptomatic intact and ruptured AAAs had similar aortic diameter, other characteristics were generally poorly reported and confounding owing to an unmeasured factor cannot be ruled out. Additionally, the CT scans of ruptured AAA cases were required to meet certain inclusion criteria in some studies and selection bias cannot be excluded.[7,11,19,26] We were unsuccessful in contacting the corresponding author of 2 studies[10,19] to clarify whether there was an overlap in participants included in these investigations. Nevertheless, the leave-one-sensitivity analysis suggested that the findings of the PWRI meta-analysis was not materially altered with individual omission of either of these studies.[10,19] Lastly the relevance of the findings of this meta-analysis to small AAAs is limited as 5 studies included only patients with large AAAs[7,11,19,20,26] (mean±SD aortic diameter [mm] ranged between 71±15 and 82±14 for the asymptomatic intact AAAs; 72±18 and 82±13 for the ruptured AAAs). Furthermore, this meta-analysis compared PWS and PWRI in individuals with asymptomatic intact and ruptured AAAs but did not examine the predictive ability of these biomechanical measures for AAA rupture. Investigating this would require a large observational study; however, owing to the low rupture rate of small AAAs and the high repair rate of large AAAs, such a study maybe infeasible to perform.

CONCLUSIONS

In conclusion the results of this study suggest that PWRI is greater in ruptured than asymptomatic intact AAAs of similar diameter. The findings suggest the potential value of biomechanical measures in estimating AAA rupture risk accepting the medium to high risk of bias of the included studies.

ARTICLE INFORMATION

Received October 13, 2020; accepted February 19, 2021.

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Sources of Funding

The Townsville Hospital and Health Services Study, Education and Research Trust Fund and The Queensland Government supported this work. Jonathan Golledge holds a Practitioner Fellowship from the National Health and Medical Research Council (1117061) and a Senior Clinical Research Fellowship from the Queensland Government, Australia. Joseph V. Moxon holds an Advance Queensland Mid-Career fellowship from the Queensland Government. Singh holds a Junior Doctor Research Fellowship from the Queensland Government.

Disclosures

T. Christian Gasser is a scientific advisor for VASCOPS GmbH. The remaining authors have no disclosures to report.

Supplementary Material

Data S1
Table S1
Figures S1–S3

REFERENCES

1. Golledge J. Abdominal aortic aneurysm: update on pathogenesis and medical treatments. *Nat Rev Cardiol*. 2019;16:225–242. DOI: 10.1038/s41569-018-0114-9.
2. Sampson UK, Norman PE, Fowkes FGR, Aboyans V, Song Y, Harrell FE Jr, Forouzanfar MH, Naghavi M, Denenberg JO, McDermott MM. Global and regional burden of aortic dissection and aneurysms: mortality trends in 21 world regions, 1990 to 2010. *Glob Heart*. 2014;9:171–180.e110. DOI: 10.1016/j.gheart.2013.12.010.
3. Khosla S, Morris D, Moxon J, Walker PJ, Gasser T, Golledge J. Meta-analysis of peak wall stress in ruptured, symptomatic and intact abdominal aortic aneurysms. *Br J Surg*. 2014;101:1350–1357. DOI: 10.1002/bjs.9578.
4. The UK Small Aneurysm Trial Participants. Mortality results for randomised controlled trial of early elective surgery or ultrasonographic surveillance for small abdominal aortic aneurysms. *Lancet*. 1998;352:1649–1655.
5. Wanhainen A, Verzini F, Van Herzeele I, Allaire E, Bown M, Cohnert T, Dick F, van Herwaarden J, Karkos C, Koelemay M, et al. Editor's choice–European Society for Vascular Surgery (ESVS) 2019 clinical practice guidelines on the management of abdominal aorto-iliac artery aneurysms. *Eur J Vasc Endovasc Surg*. 2019;57:8–93. DOI: 10.1016/j.ejvs.2018.09.020.
6. Cao P, De Rango P, Verzini F, Parlani G, Romano L, Cieri E; Group CT. Comparison of surveillance versus aortic endografting for small aneurysm repair (CAESAR): results from a randomised trial. *Eur J Vasc Endovasc Surg*. 2011;41:13–25. DOI: 10.1016/j.ejvs.2010.08.026.

7. Singh TPMJ, Iyer V, Gasser T, Jenkins J, Golledge J. Comparison of peak wall stress and peak wall rupture index in ruptured and asymptomatic intact abdominal aortic aneurysms (accepted). *Br J Surg*. 2020. Sep 30. [epub ahead of print]. DOI: 10.1002/bjs.11995.
8. Leemans EL, Willems TP, van der Laan MJ, Slump CH, Zeebregts CJ. Biomechanical indices for rupture risk estimation in abdominal aortic aneurysms. *J Endovasc Ther*. 2017;24:254–261. DOI: 10.1177/1526602816680088.
9. Indrakusuma R, Jalalzadeh H, Planken R, Marquering H, Legemate D, Koelemay M, Balm R. Biomechanical imaging markers as predictors of abdominal aortic aneurysm growth or rupture: a systematic review. *Eur J Vasc Endovasc Surg*. 2016;52:475–486. DOI: 10.1016/j.ejvs.2016.07.003.
10. Siika A, Lindquist Liljeqvist M, Zommorodi S, Nilsson O, Andersson P, Gasser TC, Roy J, Hultgren R. A large proportion of patients with small ruptured abdominal aortic aneurysms are women and have chronic obstructive pulmonary disease. *PLoS One*. 2019;14:e0216558. DOI: 10.1371/journal.pone.0216558.
11. Leemans EL, Willems TP, Slump CH, van der Laan MJ, Zeebregts CJ. Additional value of biomechanical indices based on cta for rupture risk assessment of abdominal aortic aneurysms. *PLoS One*. 2018;13:e0202672. DOI: 10.1371/journal.pone.0202672.
12. Moher D, Liberati A, Tetzlaff J, Altman DG; Group P. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med*. 2009;6:e1000097. DOI: 10.1371/journal.pmed.1000097.
13. Kmet LM, Cook LS, Lee RC. *Standard Quality Assessment Criteria for Evaluating Primary Research Papers From a Variety of Fields*. Canada: Alberta Heritage Foundation for Medical Research Edmonton; 2004. Available at: https://www.ihe.ca/advanced-search/standard-quality-assessment-criteria-for-evaluating-primary-research-papers-from-a-variety-of-fields. Accessed September 10, 2020.
14. Stang A. Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. *Eur J Epidemiol*. 2010;25:603–605. DOI: 10.1007/s10654-010-9491-z.
15. Mantel N, Haenszel W. Statistical aspects of the analysis of data from retrospective studies of disease. *J Natl Cancer Inst*. 1959;22:719–748.
16. Truijers M, Pol J, Schultzekool L, Van Sterkenburg S, Fillinger M, Blankensteijn J. Wall stress analysis in small asymptomatic, symptomatic and ruptured abdominal aortic aneurysms. *Eur J Vasc Endovasc Surg*. 2007;33:401–407. DOI: 10.1016/j.ejvs.2006.10.009.
17. Higgins JP, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA. *Cochrane Handbook for Systematic Reviews of Interventions*. Chichester: John Wiley & Sons; 2019.
18. Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. *Stat Med*. 2002;21:1539–1558. DOI: 10.1002/sim.1186.
19. Siika A, Lindquist Liljeqvist M, Hultgren R, Gasser TC, Roy J. Aortic lumen area is increased in ruptured abdominal aortic aneurysms and correlates to biomechanical rupture risk. *J Endovasc Ther*. 2018;25:750–756. DOI: 10.1177/1526602818808292.
20. Polzer S, Gasser TC. Biomechanical rupture risk assessment of abdominal aortic aneurysms based on a novel probabilistic rupture risk index. *J R Soc Interface*. 2015;12:20150852. DOI: 10.1098/rsif.2015.0852.
21. Sterne JA, Gavaghan D, Egger M. Publication and related bias in meta-analysis: power of statistical tests and prevalence in the literature. *J Clin Epidemiol*. 2000;53:1119–1129. DOI: 10.1016/S0895-4356(00)00242-0.
22. Fillinger MF, Raghavan ML, Marra SP, Cronenwett JL, Kennedy FE. In vivo analysis of mechanical wall stress and abdominal aortic aneurysm rupture risk. *J Vasc Surg*. 2002;36:589–597. DOI: 10.1067/mva.2002.125478.
23. Soto B, Vila L, Dilme J, Escudero J-R, Bellmunt S, Camacho M. Finite element analysis in symptomatic and asymptomatic abdominal aortic aneurysms for aortic disease risk stratification. *Int Angiol*. 2018;37:479–485. DOI: 10.23736/S0392-9590.18.03994-9.
24. Soto B, Vila L, Dilmé JF, Escudero JR, Bellmunt S, Camacho M. Increased peak wall stress, but not maximum diameter, is associated with symptomatic abdominal aortic aneurysm. *Eur J Vasc Endovasc Surg*. 2017;54:706–711. DOI: 10.1016/j.ejvs.2017.09.010.
25. Stevens RR, Grytsan A, Biasetti J, Roy J, Lindquist Liljeqvist M, Gasser TC. Biomechanical changes during abdominal aortic aneurysm growth. *PLoS One*. 2017;12:e0187421. DOI: 10.1371/journal.pone.0187421.
26. Gasser TC, Auer M, Labruto F, Swedenborg J, Roy J. Biomechanical rupture risk assessment of abdominal aortic aneurysms: model complexity versus predictability of finite element simulations. *Eur J Vasc Endovasc Surg*. 2010;40:176–185. DOI: 10.1016/j.ejvs.2010.04.003.
27. Brady AR, Thompson SG, Fowkes FGR, Greenhalgh RM, Powell JT. Abdominal aortic aneurysm expansion: risk factors and time intervals for surveillance. *Circulation*. 2004;110:16–21. DOI: 10.1161/01.CIR.0000133279.07468.9F.
28. Lederle FA, Wilson SE, Johnson GR, Reinke DB, Littooy FN, Acher CW, Messina LM, Ballard DJ, Ansel HJ; Center CSPC. Variability in measurement of abdominal aortic aneurysms. *J Vasc Surg*. 1995;21:945–952. DOI: 10.1016/S0741-5214(95)70222-9.
29. Golledge J, Norman PE, Murphy MP, Dalman RL. Challenges and opportunities in limiting abdominal aortic aneurysm growth. *J Vasc Surg*. 2017;65:225–233. DOI: 10.1016/j.jvs.2016.08.003.
30. Raghavan M, Vorp DA. Toward a biomechanical tool to evaluate rupture potential of abdominal aortic aneurysm: identification of a finite strain constitutive model and evaluation of its applicability. *J Biomech*. 2000;33:475–482. DOI: 10.1016/S0021-9290(99)00201-8.
31. Parr A, Mclaughlin S, Mclaughlin M, Mchir JG. Aortic calcification and abdominal aortic aneurysm expansion. *Atherosclerosis*. 2009;202:350. DOI: 10.1016/j.atherosclerosis.2008.05.017.
32. Doyle BJ, Bappoo N, Syed MBJ, Forsythe RO, Powell JT, Conlisk N, Hoskins PR, McBride OMB, Shah ASV, Norman PE, et al. Biomechanical assessment predicts aneurysm related events in patients with abdominal aortic aneurysm. *Eur J Vasc Endovasc Surg*. 2020;60:365–373. DOI: 10.1016/j.ejvs.2020.02.023.

Supplemental Material

Data S1.

Protocol for the systematic review and meta-analysis

Protocol for a systematic review and meta-analysis of peak wall stress and peak wall rupture index in ruptured and asymptomatic intact abdominal aortic aneurysms.

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Background: Aortic peak wall stress (PWS) and peak wall rupture index (PWRI) are established surrogate measures of abdominal aortic aneurysm (AAA) rupture risk. Prior studies have suggested that PWS and PWRI is greater in ruptured than asymptomatic intact AAAs, although it remains unclear whether these measures confer any benefit in predicting AAA rupture compared to AAA diameter. The aim of this planned systematic review and meta-analysis is to compare PWS and PWRI in participants with ruptured and asymptomatic intact AAAs of similar diameter.

Methods: A systematic review and meta-analysis will be conducted. An electronic database search will be performed using predefined search terms to identify relevant studies. Eligible studies will be required to compare PWS and PWRI in ruptured and asymptomatic intact AAAs of similar diameter. Random-effects meta-analysis will be performed and leave-one-out sensitivity analyses will be conducted to assess the robustness of the findings. Risk of bias will be assessed using a modification of the Newcastle-Ottawa scale and standard quality assessment criteria for evaluating primary research papers.

Discussion: This meta-analysis will be the first to compare PWS and PWRI in asymptomatic intact and ruptured AAAs of similar diameter.

Introduction

Abdominal aortic aneurysm (AAA) rupture is an important cause of mortality.[1] In current clinical practice, AAA aortic diameter is the main measure used by clinicians to estimate the

risk of AAA rupture.[1, 5] Evidence from prior randomized controlled trials suggest that some large AAAs remain stable throughout a patient's lifetime, while some small AAAs can rupture.[2] This suggests that diameter is not a perfect measure of estimating the rupture risk of AAAs.[1, 5] There has been considerable interest in utilizing biomechanical measures to estimate and predict AAA rupture risk.[3, 7] Aortic peak wall stress (PWS) and peak wall rupture index (PWRI) are examples of two widely reported biomechanical indices.[7, 26] Prior meta-analyses have suggested that PWS is greater in asymptomatic intact and ruptured AAAs although the diameter in both groups were different in that analysis.[3] A meta-analysis comparing PWRI in asymptomatic intact and ruptured AAAs in individuals with similar aortic diameter has not been performed. In light of the limitations of prior studies and the paucity of pooled evidence in this area an updated systematic review and meta-analysis is required.

Systematic review question

Is PWS and PWRI greater in asymptomatic intact and ruptured AAAs of similar aortic diameter ?

Data sources search terms and search strategy

This literature review will be performed using the Web of Science (via ISI Web of Knowledge; 1965), Scopus (1966), Medline (via OvidSP, 1966) and The Cochrane Library. A combination of the following search terms will be used: "peak wall stress" OR "peak wall rupture index" OR "rupture potential index" AND "abdominal aortic aneurysm". Specific search criteria database are reported below:

Medline (via OvidSP, 1966): ((peak wall stress) OR (peak wall rupture index)) AND (abdominal aortic aneurysm) [Across all fields]

Web of Science (via ISI Web of Knowledge; 1965): (((peak wall stress) OR (peak wall rupture index)) AND (abdominal aortic aneurysm)) Timespan: All years. Indexes: SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI, CCR-EXPANDED, IC.

Scopus (1966): TITLE-ABS-KEY (((peak AND wall AND stress) OR (peak AND wall AND rupture AND index)) AND (abdominal AND aortic AND aneurysm))

The Cochrane Library: peak wall stress in All Text OR peak wall rupture index in Title Abstract Keyword AND abdominal aortic aneurysm in Title Abstract Keyword - (Word variations have been searched)

Inclusion and exclusion criteria

Case-control studies investigating PWS in patients with ruptured and diameter matched asymptomatic intact AAAs. Eligible studies should be of case-control design. The AAA diameter between asymptomatic intact and ruptured groups should be similar (within 3mm mean difference). Studies that include symptomatic AAA patients in the ruptured group will be excluded. To avoid double-counting of data, the study population in a given publication should not have been used in a previous study of those included in the review.

Data extraction (selection and coding)

Data will be extracted by three authors independently (TS, JM and JG). The following data will be collected: Sample sizes for the ruptured and asymptomatic intact AAA group, study design, software used to perform finite element analysis (FEA), PWS and PWRI estimates, AAA diameter, risk factors (including age, sex, smoking history, hypertension, diabetes, ischaemic heart disease [IHD], stroke, chronic obstructive pulmonary disease [COPD]) and systolic blood pressure. If relevant data is not reported in the publication, the corresponding will be contacted via email.

Assessment of methodological quality (risk of bias)

A quality assessment tool has been created to assess the risk of bias of the included studies. This tool was created by the authors and incorporates components of two widely reported quality assessment tools (Newcastle-Ottawa scale and Standard quality assessment criteria for evaluating primary research papers).[13, 14] A number of additional criteria relevant to this systematic review will also be included. This includes: criteria used to define AAA rupture; reporting of the method used to estimate PWS and PWRI and reproducibility; use of a standardised blood pressure in PWS and PWRI calculations (i.e. use of a single blood pressure measurement for all participants or omission of blood pressure in calculations); inclusion of CT scan prior to or after rupture (for ruptured cases); matching for AAA diameter between asymptomatic intact and ruptured cases; matching for other confounding variables. The overall risk of bias assessed within each study will be assessed as low, medium or high based on predefined criteria. Please see Supplementary Table 1 for further details regarding the quality assessment tool.

Approach to meta-analysis

Meta-analyses will be performed using inverse variance-weighted methods.[15] Standardised mean differences (SMD) with 95% confidence intervals (CI) will be calculated for both PWS and PWRI pooled estimates. Previous meta-analyses have identified there is no standardised method of computing PWS and PWRI and therefore SMDs will be calculated using random-effects weighting to account for likely inter-study methodological heterogeneity.[17] PWS outcome data will be converted from Newton Per Square Centimeter (N/cm^2) to kilopascal (kPa) where required to ensure that units are consistent for the meta-analysis.[16] Inter-study heterogeneity will be assessed using the I^2 index and values <25%, between 25-75% and >75% will be considered to represent low, moderate and high heterogeneity, respectively.[17] If PWS and PWRI are computed at a standardised blood pressure (i.e single blood pressure for

all participants) this value will be used in the meta-analysis. If a standardised blood pressure is not used, PWS and PWRI calculated at patient specific blood pressures will be used. To identify sources of heterogeneity a leave-one-out-sensitivity analysis will be planned. This will involve excluding individual studies one at a time and recalculating the pooled estimates for the remaining studies. Publication bias will be assessed by funnel plots comparing the summary estimate of each study to its precision (1/standard error) for outcomes that are reported in ≥5 studies.[21] Analyses will be conducted using Stata version 16.1 (StataCorp LP, College Station, Texas, USA). All statistical tests will be two-sided and a p-value of <0.05 will be considered significant.

Ethics and dissemination

Ethical approval is not required for this systematic review and meta-analysis as data already available in scientific databases will be analysed. The results of this review will be submitted for peer-reviewed publication and findings will be presented at conferences.

Table S1. Criteria used to perform the assessment of methodological quality.

Quality assessment				
Category	**Criteria**	**Response**		
		Yes	Partial	No
Clearly defined objective?	Clear hypothesis stated and tested. Objective easily identified in introductory section (or first paragraph of methods section). • Specifies all the following: purpose, subjects/target population, and the specific association(s)/descriptive parameter(s) under the investigation.	X		
	Vaguely/incompletely reported (e.g. "describe the effect of" or "examine the role of") OR substantial information must be collected from parts of the paper other than introduction/background/objective section.		X	
	Question or objective is not reported or is incomprehensible.			X
Prospective study design?	Hypothesis designed prior to selection of participants.	X		
	• Hypothesis and selection criteria designed after the occurrence of respective endpoints (e.g. AAA rupture). • Data collection conducted retrospectively after participants experienced outcomes of interest (e.g AAA rupture)			X
Selection criteria well described?	Selection strategy designed to obtain an unbiased sample of the relevant target population. • Methods for selection/recruitment/sampling reported in the study. • Definition of AAA adequately described (appropriate investigations used including ultrasound, angiography, or clinical assessment by a vascular specialist, or scheduled surgical repair of AAA etc.)	X		

	• At least 3 of the specified exclusion criteria described [listed below]			
	Selection methods (and inclusion/exclusion criteria) are not completely described OR selection methods described elsewhere. • Included patients who have either an intact OR ruptured AAA AND no previous endovascular or open surgical repair • Available CT scan of non-ruptured AAA OR • Available CT scan of ruptured AAA at the time of rupture prior to any surgical intervention. • Excluded patients where there was no CT scan of the AAA available for analysis. • Excluded patients where poor quality of CT scans or technical factors (e.g. extreme vessel wall angulation; contrast extravasation) precluded PWS/PWRI estimation.		X	
	No information provided; OR obviously inappropriate selection procedures.			X
Was an objective definition of AAA rupture utilised?	Appropriate definition of AAA rupture used including both of the following criteria: • Diagnosis of a ruptured AAA by a consultant vascular physician/surgeon • AAA associated with objective evidence of blood within the peritoneum identified on a CT scan or alternate imaging modality	X		
	Limited definition of ruptured AAA described: • Definition restricted to diagnosis by consultant vascular physician/surgeon OR • Definition restricted to diagnosis on imaging, but no description of radiological findings to support diagnosis of ruptured AAA • AAA rupture diagnosis based on electronic coding		X	

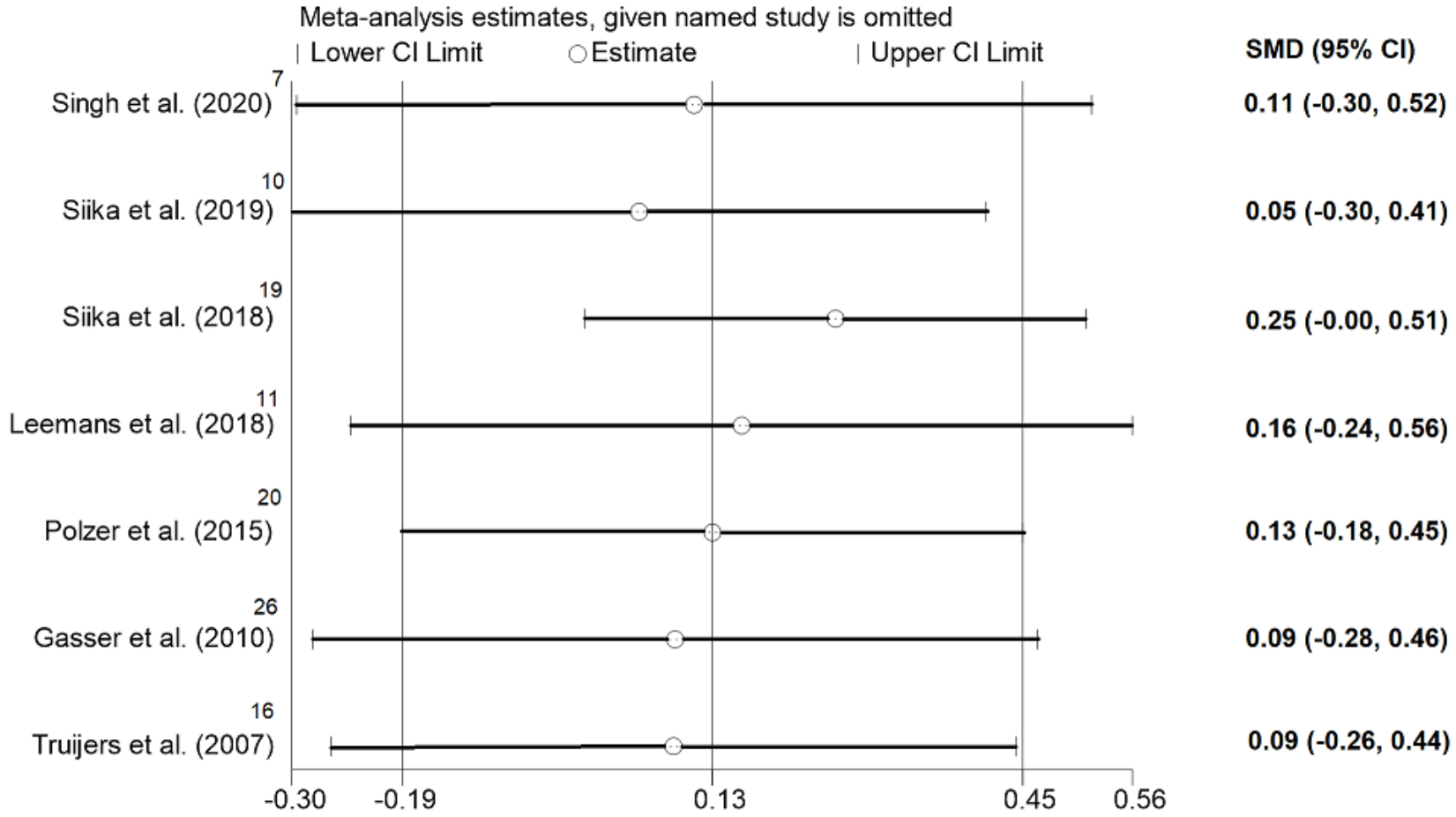
	No definition of ruptured AAA described			X
Assessment of outcome – Method of estimating PWS and PWRI well described	Method of estimating PWS and PWRI well described and: • Reproducibility evaluated and reported within paper AND • Reproducibility determined to be moderate-high	X		
	Method of estimating ILT well described: • no assessment of reproducibility reported OR • Reproducibility determined to be low		X	
	Method of estimating ILT not described OR limited description provided AND no assessment of reproducibility made			X
Standardised blood pressure used for PWS/PWRI measurements?	A standard blood pressure (e.g 140/80 mmHg) was used to compute PWS and PWRI measurements for all patients	X		
	Patient specific blood pressure (at the time of CT scan) was used to perform PWS/PWRI measurements			X
Sample size calculation/estimation reported in methodology.	Details of sample size calculation/estimation reported in methodology	X		
	Required sample size reported, but no details on how this was calculated/estimated		X	
	No sample size calculation/estimation conducted			X
What was the sample size?	<50 OR 50-100 OR >100	N/A	N/A	N/A
	Not reported	N/A	N/A	N/A

Did participants with AAA rupture undergo a CT scan prior rupture and after rupture	For all patients, CT data were present both before and during the rupture event.	X		
				X
Were participant characteristics adequately described?	Sufficient relevant baseline information clearly characterising the participants are provided (or reference to previously published baseline data is provided). Includes at least 5 of the following: • Age, Gender, AAA diameter (mm), smoking, HTN, diabetes, coronary artery disease, statin prescription, aspirin prescription.	X		
	Poorly defined criteria or incomplete relevant baseline / demographic information (e.g. Information on likely confounders not reported). • Includes less than 5 of the characteristics reported above.		X	
	No baseline / demographic information provided.			X
Were participants in the ruptured and intact AAA groups matched for diameter?	To provide an objective comparison of ruptured and intact AAAs, both groups were matched for maximum diameter.	X		
				X
Was participants matched for other confounding factors for AAA rupture?	Matching undertaken or adjustments are made for at least 2 of the following variables: • Age, sex, HTN, smoking and diabetes	X		
	Did not meet the criteria above OR did not specify which variables were adjusted or matched for		X	

	No adjustment or matching undertaken for confounding factors other than maximum diameter			X

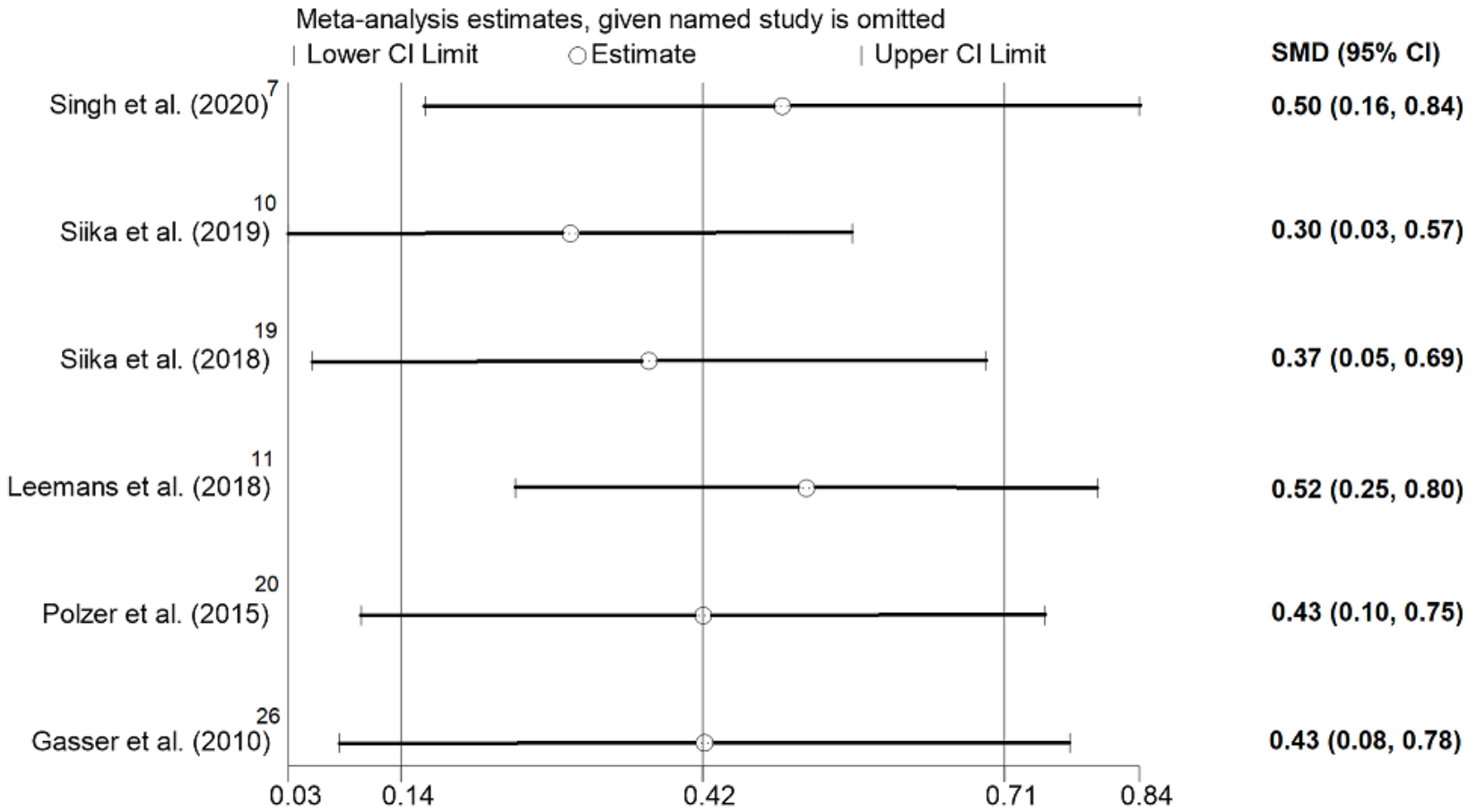
Overall risk of bias within study	**Criteria**
Low	>10 criteria with 'Yes' response and sample size > 100
Medium	>5 and ≤10 criteria with 'Yes' response and sample size between 50-100
High	≤5 criteria 'Yes' response and sample size between <50 or between 50-100.

Figure S1. Leave-one-out sensitivity analysis for the meta-analysis of PWS in asymptomatic intact and ruptured AAAs.



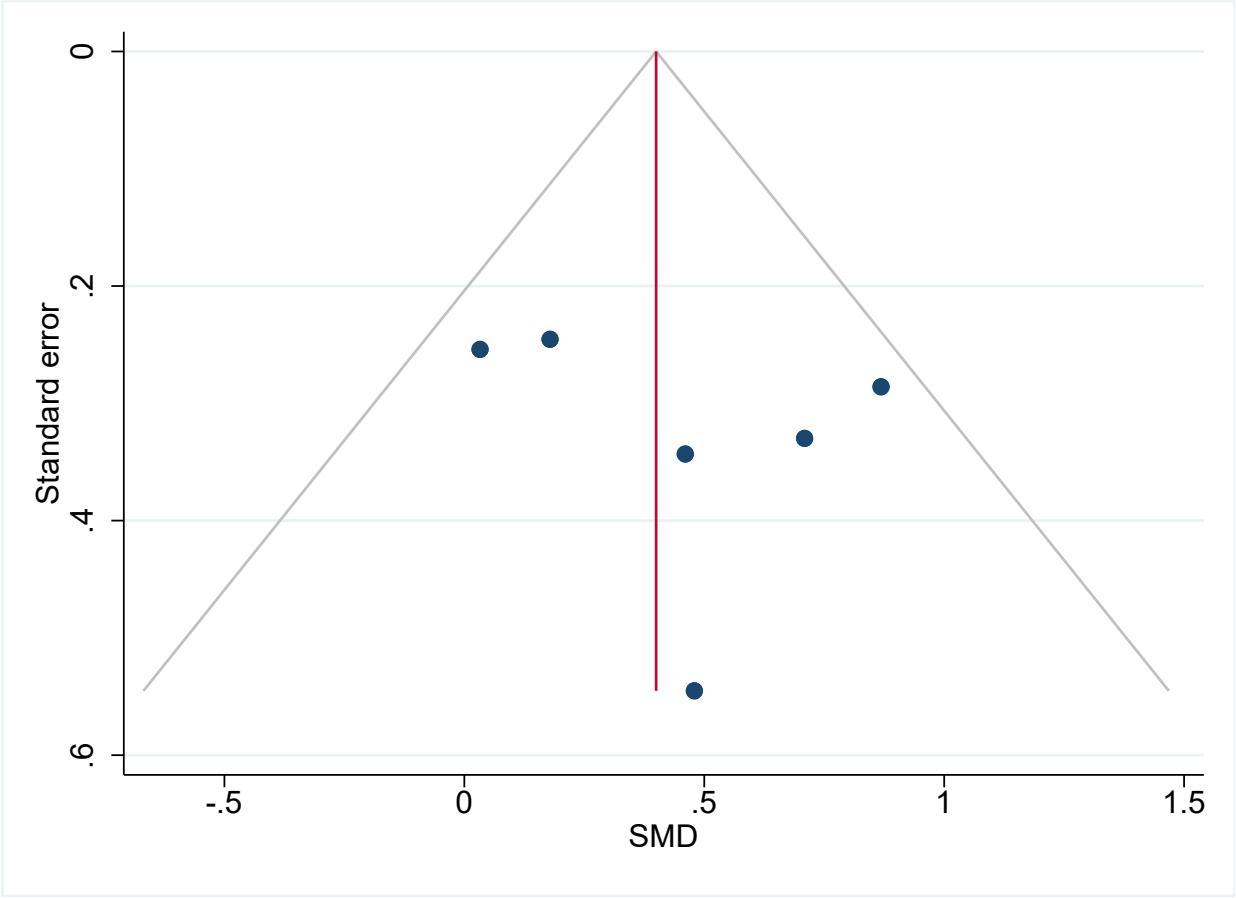
SMD, standardised mean difference; CI, confidence intervals. Indicates the pooled results with the corresponding study excluded from the analysis.

Figure S2. Leave-one-out sensitivity analysis for the meta-analysis of PWRI in asymptomatic intact and ruptured AAAs.



SMD, standardised mean difference; CI, confidence intervals. Indicates the pooled results with the corresponding study excluded from the analysis.

Figure S3. Funnel plot with pseudo 95% CIs of the difference in PWRI between ruptured and asymptomatic intact AAAs.



SMD, standardised mean difference; PWRI, peak wall rupture index; CI, confidence intervals.