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Review article

High ankle-brachial index and risk of cardiovascular or all-cause mortality: A meta-analysis

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HIGHLIGHTS

- Predictive values of abnormally high ankle-brachial index (ABI) for mortality are controversial.
- High ABI is independently associated with an increased risk of all-cause mortality.
- Routine measurement of ABI can identify persons who are at high risk of death.

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ABSTRACT

Background and aims: Studies on high ankle-brachial index (ABI) to predict mortality risk have yielded conflicting results. This meta-analysis aimed to evaluate the association between abnormally high ABI and risk of cardiovascular or all-cause mortality.

Methods: Pubmed and Embase databases were systematically searched for relevant articles published up to August 15, 2018. Longitudinal observational studies that evaluated the association between abnormally high ABI at baseline and risk of cardiovascular or all-cause mortality were included. Pooled results were expressed as risk ratio (RR) with 95% confidence intervals (CI) for the abnormal high *versus* the reference normal ABI category.

Results: Eighteen studies enrolling 60,467 participants were included. Abnormally high ABI was associated with an increased risk of all-cause mortality (RR 1.50; 95% CI 1.27–1.77) and cardiovascular mortality (RR 1.84; 95% CI 1.54–2.20). The pooled RR of all-cause mortality was 1.45 (95% CI 1.16–1.82) for the general population, 1.67 (95% CI 1.03–2.71) for chronic kidney disease (CKD)/hemodialysis patients, and 1.55 (95% CI 1.10–2.20) for suspected or established cardiovascular disease (CVD) patients, respectively. The pooled RR of cardiovascular mortality was 1.84 (95% CI 1.43–2.38) for the general population, 4.28 (95% CI 2.18–8.40) for CKD/hemodialysis patients, and 1.58 (95% CI 1.22–2.05) for suspected or established CVD patients, respectively.

Conclusions: Abnormally high ABI is independently associated with an increased risk of all-cause mortality. However, interpretation of the association between abnormally high ABI and cardiovascular mortality should be done with caution because of the likelihood of publication bias.

1. Introduction

Ankle-brachial index (ABI) is defined by the ratio of ankle and brachial systolic blood pressure [1]. Clinically, ABI value of ≤0.90 is used to diagnose peripheral artery disease [2]. A well-designed meta-analysis [3] suggested that low ABI less than 0.9 was an independent predictor of cardiovascular or all-cause mortality in the general population. High ABI is commonly correlated with arterial calcification [4] and may be a marker of increased vascular stiffness [5]. In the general population, overall prevalence of high ABI (> 1.4) was 7.6% among 9647 subjects with age ranging from 30 to 80 years [6]. There is controversy on the predictive significance of an abnormally high ABI. A number of studies [7–12] but not all [13–24] have shown that abnormally high ABI was also associated with an increased risk of cardiovascular or all-cause mortality. These inconsistent findings may be partly correlated with different protocol of ABI measurement or heterogeneous populations.

To the best of our knowledge, these available meta-analyses [25,26]

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mainly evaluated the effect of low ABI on health outcomes. No previous meta-analysis has evaluated the association between high ABI and mortality risk. Therefore, we performed this meta-analysis of the longitudinal observational studies to evaluate the association between abnormally high ABI and risk of cardiovascular or all-cause mortality.

2. Materials and methods

We performed and reported this meta-analysis according to the guidelines of the Meta-analysis Of Observational Studies in Epidemiology statement [27]. Pubmed and Embase databases were systematically searched for pertinent articles published until August 15, 2018. The following search keywords were used in various combinations: “ankle-brachial index” OR “ankle brachial pressure index” OR “ankle-arm blood pressure index” AND “mortality” OR “death” AND “follow-up” OR “longitudinal”. In addition, we manually screened reference lists of relevant studies to identify potentially eligible articles. All literature searches were restricted in English language.

Two authors independently selected the articles according to the following inclusion criteria: 1) original longitudinal observational study; 2) measurement of ABI at baseline; 3) provided multivariate adjusted risk ratio (RR) or hazard ratio (HR) with 95% confidence intervals (CI) of cardiovascular or all-cause mortality for the abnormally high ABI *versus* the normal ABI. Abnormally high ABI (>1.3 or >1.4) was defined by the individual studies. Articles reporting the cardiovascular or all-cause mortality by a single cutoff ABI value were excluded.

The following data were collected by two independent authors: surname of the first author, publication year, origin of study, study design, study population, number of participants, percentage of male gender, age of participants, cutoff value of high ABI, outcome measure, event number, fully adjusted RR or HR with 95%CI, follow-up time, and reported confounders in multivariate model. We assessed the methodological quality of the included studies using the Newcastle–Ottawa Scale (NOS) [28]. This scale evaluated the selection bias, detection bias, and attrition bias. Study with a score of ≥ 7 stars was considered to be of good quality. Any disagreements in data extraction and quality assessment were resolved by consensus.

All the meta-analyses were performed by STATA 12.0 (STATA Corp LP, College Station, TX, USA). Because of no uniform definition of abnormally high ABI, participants were allocated to the high ABI category according to cutoff values reported by individual studies. The pooled risk estimate of cardiovascular or all-cause mortality was calculated for the abnormally high ABI *versus* the reference normal ABI category. Heterogeneity across studies was assessed using the Cochrane *Q* test (significance level of $p < 0.10$) and the I^2 statistic (significance level $> 50\%$). A random effect model was used to pool the summary effect when significant heterogeneity was found; otherwise, we selected a fixed-effect model. The presence of publication bias was evaluated by the Begg's test [29], Egger's test [30], and the funnel plot. Moreover, a “trim-and-fill” method was used to check the possible influence of publication bias. Sensitivity analysis was performed by sequentially omitting one study at each time. Subgroup analyses were conducted according to the study population, study type, sample size, follow-up time, and whether adjustment for classic cardiovascular risk factors.

3. Results

Fig. 1 shows a flow chart outlining the study selection process. We identified 2211 relevant articles from the initial literature search. After extensive review, 18 studies were ultimately included in this meta-analysis. The main characteristics of the included studies are described in Table 1. In total, these eligible studies enrolled 60,467 individuals. The number of participants ranged from 219 to 7542. The percentage of men varied from 43.7% to 89.0%. Follow-up duration ranged between 1.0 year and 11.1 years. Of 18 studies, 5 studies [8,13,14,17,23] enrolled the participants from the general population, 5 studies [7,9,12,20,24] enrolled CKD/hemodialysis patients,7 studies [10,15,16,18,19,21,22] enrolled the suspected/established cardiovascular disease patients, and one study [11] included the hospitalized medical patients. All the selected studies were classified as moderate to good quality ranking with 6–8 points.

Seventeen studies [7–17,19–24] evaluated the association between abnormally high ABI and all-cause mortality risk. As shown in Fig. 2, a random effect model meta-analysis showed abnormally high ABI was associated with an increased risk of all-cause mortality (RR 1.50; 95% CI 1.27–1.77; $I^2 = 49.9\%$, $p = 0.010$) than the reference normal ABI. The likelihood of publication bias was low according to the visual inspection of funnel plot (Supplemental Fig. S1). The Begg's test ($p = 0.232$) and Egger's test ($p = 0.864$) further confirmed no evidence of publication bias. In addition, the “trim-and-fill” approach indicated that imputing one potential missing study did not change the original significant association (RR 1.52; 95% CI 1.02–2.26). Sensitivity analysis by sequential exclusion of individual studies did not significantly change the overall risk estimate (data not shown).

Cardiovascular mortality outcome was reported in 15 studies [7–15,17–19,21–23]. As shown in Fig. 3, a fixed-effect model meta-analysis indicated abnormally high ABI was associated with an increased risk of cardiovascular mortality (RR 1.83; 95%CI 1.55–2.18; $I^2 = 5.4\%$, $p = 0.392$) than the reference normal ABI. The likelihood of publication bias was found in the asymmetric funnel plot and Begg's test ($p = 0.038$) but not in the Egger's test ($p = 0.132$). The “trim-and-fill” approach showed that imputing three potential missing studies altered the original significant association (RR 1.73; 95% CI 0.92–3.26). Sensitivity analysis by sequential removal of any single study did not significantly alter the pooled risk estimate (data not shown).

Results of subgroup analysis are shows in Table 2. The pooled RR of all-cause mortality was 1.45 (95% CI 1.16–1.82) for the general population, 1.67 (95% CI 1.03–2.71) for CKD/hemodialysis patients, and 1.55 (95% CI 1.10–2.20) for suspected or established cardiovascular disease patients, respectively. Similarity, the pooled RR of cardiovascular mortality was 1.84 (95% CI 1.43–2.38) for the general population, 4.28 (95% CI 2.18–8.40) for CKD/hemodialysis patients, and 1.58 (95% CI 1.22–2.05) for suspected or established cardiovascular disease patients, respectively. Moreover, the association of abnormal high ABI with high risk of all-cause and cardiovascular mortality was consistently observed in each named subgroups.

4. Discussion

This meta-analysis suggested that abnormally high ABI was possibly associated with an increased risk of cardiovascular and all-cause mortality in heterogeneous populations. Individuals with abnormally high ABI had an 84% and 45% higher risk of cardiovascular and all-cause mortality in the general population. CKD/hemodialysis patients with high ABI had a 4.28-fold and 67% higher risk of cardiovascular and all-cause mortality. In patients with suspected or established cardiovascular disease, abnormally high ABI was associated with 58% and 55% higher risk of cardiovascular and all-cause mortality.

According to the ACCF/AHA guidelines, ABI is commonly defined as low (< 0.9), normal (0.9–1.4) and high (> 1.4) [31]. However, most studies regarding the association of ABI with mortality risk mainly focused on the low ABI. European Guidelines on cardiovascular disease prevention in clinical practice suggest that low ABI is inversely related

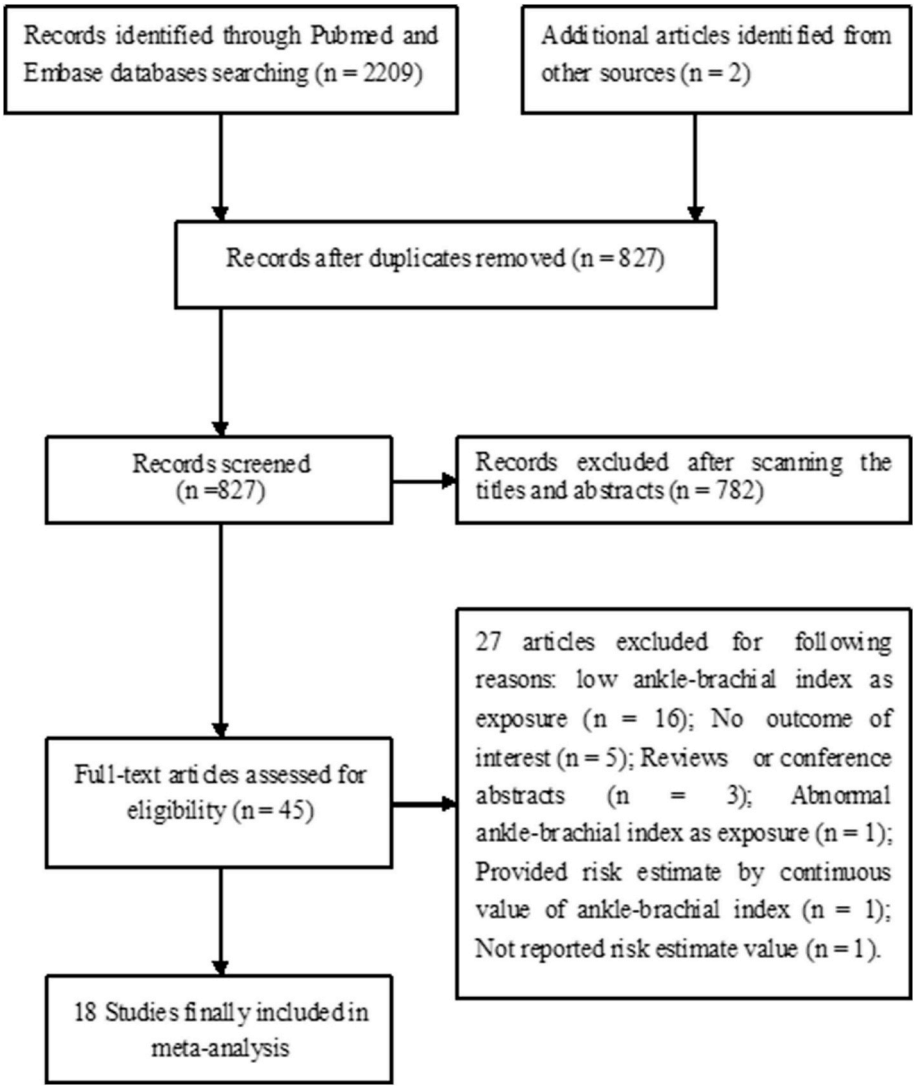

Fig. 1. Flow chart showing the study selection process.

to cardiovascular risk and predicts further development of angina, myocardial infarction, congestive heart failure, coronary artery bypass graft surgery, and stroke [32,33]. A previous meta-analysis of observational cohort studies [25] confirmed that a low ABI was an associated with an increased risk of subsequent cardiovascular and cerebrovascular morbidity and mortality. In comparison, our study is the first meta-analysis to evaluate the role of high ABI for predicting cardiovascular and all-cause mortality risk. A recently published individual participant data meta-analysis [34] supported that high ABI was significantly associated with an increased risk of all-cause mortality in the Japanese population. Together these findings, there was a U-shaped association between ABI and cardiovascular and all-cause mortality.

Patients with end-stage renal disease undergoing hemodialysis had a substantially higher risk of death [35,36]. Cardiovascular events are the main cause of mortality in hemodialysis patients [37]. Therefore, risk stratification of mortality is crucial among these patients. High ABI is usually associated with neuropathy and/or CKD [21]. In our meta-analysis, the predictive value of high ABI for cardiovascular mortality was stronger (4.28-fold) in the CKD/hemodialysis patients. This finding reveals that CKD/hemodialysis patients with high ABI may benefit from more intensive therapeutic intervention to improve survival.

The mechanisms underlying the association between high ABI and mortality remain uncertain. One possible explanation is that the high ABI is an indicator of medial arterial calcification [38] and reflects generalized arterial stiffness [39]. Arterial stiffness likely contributes to the association.

It should be noted that the current findings are challenged by diabetes (as a diagnosis, with/without insulin, diabetes duration or glycemic control), since diabetes is also associated strongly with medial calcification – Mönckeberg's mediasclerosis [39]. Therefore, diabetes may be an important confounding factor in accounting for the predictive role of high ABI. Future studies investigating the predictive role of high ABI by diabetic status are highly recommended.

This meta-analysis had several limitations. First, this is a study level but not individual participants' meta-analysis and included participants were heterogeneous populations. Second, results of subgroup analyses may be not reliable due to relatively small number of studies included. Third, ABI was evaluated based on a single measurement, which may potentially result in selection bias of participants. Repeated measurements of ABI are warranted, particularly for those with longer follow-up duration. Fourth, the likelihood of publication bias was observed for the cardiovascular mortality outcome and therefore interpretation of the association between abnormally high ABI and cardiovascular mortality

Table 1
Summary of studies included in the meta-analysis.

Author/year	Region	Design	Study population	Sample size (% male)	Age (years)	Normal ABI	High ABI	No. events OR/HR (95% CI)	Follow-up (years)	Adjustment for covariates	Overall NOS
Ono 2003 [7]	Japan	Prospective cohort study	Hemodialysis	1010 (63.5)	60.6 ± 12.5	0.9–1.3	≥1.3	Total death:118 2.33 (1.11–4.89); CV death:77 3.04 (1.14–8.12)	2	Age, DM, history of CVD, DBP, pulse pressure, albumin, creatinine, TC, and Kt/V	7
Resnick 2004 [8]	USA	Prospective cohort study	General population	4393 (59.3)	45–74	0.9–1.4	> 1.4	Total death:1022 1.77 (1.48–2.13); CV death:272 2.09 (1.49–2.94)	8.3	Age, gender, DM, lipids, hypertension, renal function, and fibrinogen	8
O'Hare 2006 [14]	USA	Prospective cohort study	General population	5748 (43)	73 ± 6	1.11–1.2	> 1.4	Total death:2311 1.57 (1.07–2.31); CV death:953 1.76 (0.97–3.18)	11.1	Age, gender, race, DM, creatinine, BMI, LDL cholesterol, HDL, smoking, CRP, SBP, DBP, antihypertensive medications, TG, prevalent CAD, stroke, and congestive heart failure	8
Sutton-Tyrrell 2008 [13]	USA	Prospective cohort study	General population	2886 (48.3)	70 to 79	0.9–1.3	≥1.31	Total death:616 1.05 (0.70–1.57); CV death:219 1.32 (0.66–2.63)	6.7	Age, gender, race, SBP, site, prevalent CVD, DM, BMI, smoking, PA, TC, HDL, and TG	8
Chen 2010 [9]	Taiwan	Prospective study	Stages 3–5 of CKD and hemodialysis	400 (53.8)	62.3 ± 13.5	0.9–1.3	≥1.3	Total death:48 3.85 (1.04–14.2) CV death:20 4.51 (1.13–18.00)	1.9	Age, sex, presence of CAD and hemodialysis, DBP, albumin, fasting glucose, TC, LDL and eGFR	7
Suominen 2010 [15]	Finland	Retrospective study	Suspected PAD	1261 (58.4)	69.7 ± 11.8	0.9–1.3	≥1.3	Total death:576 2.25 (1.51–3.35); CV death:298 1.64 (0.97–2.75)	3.25	Age, sex, DM, hyperlipidemia, hypertension, smoking, CHD, cerebrovascular disease, respiratory disease, chronic renal failure	7
Manzano 2010 [10]	Spain	Prospective cohort study	Stable coronary and/or cerebrovascular disease	1096 (65.2)	73.6 ± 5.4	0.9–1.4	> 1.4	Total death:84 3.53 (1.64–7.58); CV death:60 3.18 (1.20–8.41)	1.0	Age, DM, blood pressure, albuminuria, coronary disease, antiplatelet treatments, and left ventricular hypertrophy	6
Abbott 2012 [16]	Multination	Retrospective study	Stable CAD in patients with T2D	2240 (71.4)	62.4 ± 8.9	0.9–1.3	> 1.3	Total death:316 1.31 (0.84–2.05);	5.3	Age, sex, race, duration of DM, BMI, insulin therapy, HbA1c, smoking, hypertension, LVEF, CKD, hypercholesterolemia, albumin/creatinine, CRP, history of CHF, peripheral neuropathy, myocardial jeopardy, angina, and diseased regions	7
Pasqualini 2012 [11]	Italy	Prospective study	Hospitalized medical patients	707 (46)	74.7 ± 10	0.9–1.4	> 1.4	Total death:163 1.77 (1.03–3.05); CV death:63 2.13 (1.03–4.68)	1.6	Age, gender, BMI, smoking, DM, SBP, TC, creatinine, treatment with statins and with antiplatelet drugs, and major comorbidities	7
Adragao 2012 [12]	Portugal	Prospective study	Hemodialysis	219 (60)	65 ± 15	1.1–1.3	> 1.3	Total death:50 2.71 (1.06–6.93) CV death:29 7.15 (2.05–24.86)	2.4	Age, hemodialysis duration, DM, vascular disease at baseline, and phosphorus level	6
Alzamora 2013 [17]	Spain	Prospective cohort	General population	3307 (43.7)	64.2 ± 8.7	0.9–1.4	≥1.4	Total death:124 1.0 (0.50–2.0); CV death:29 1.2 (0.30–5.10)	4.03	Age, sex, smoking, central and general obesity, hypertension, hypercholesterolemia, and DM	8
Hyun 2014 [18]	USA	Prospective study	Suspected atherosclerotic PAD	469 (89%)	68 ± 9	0.9–1.3	> 1.3	CV death:158 1.81 (0.77–4.24)	7.0	Age, sex, ethnicity, DM, smoking, SBP, blood pressure medication use, TC, HDL, cholesterol medication use, eGFR, and BMI	8

(*continued on next page*)

Table 1 (*continued*)

Author/year	Region	Design	Study population	Sample size (% male)	Age (years)	Normal ABI	High ABI	No. events OR/HR (95% CI)	Follow-up (years)	Adjustment for covariates	Overall NOS
Potier 2015 [19]	Multination	Prospective cohort study	Stable outpatients at high CV risk	6986 (74.2)	≥45	0.9–1.3	≥1.3	Total death:695 1.38 (0.85–2.23); CV death:452 1.52 (0.86–2.68)	4.0	Age, sex, DM, smoking, BMI, history of AF, heart failure, cardiovascular events within one year, number of vascular beds with clinical disease, and use of statins and aspirin	8
Chen 2016 [20]	USA	Prospective cohort study	CKD	3627 (54.0)	58.1 ± 11.1	1.0–1.4	≥1.4	Total death:712 1.00 (0.62–1.62)	7.5	Age, race, sex, clinic site, history of CVD, DM, hypertension, BMI, smoking, alcohol, education, SBP, LDL, HDL, glucose, hs-CRP, 24-h albuminuria, eGFR, and use of ACEIs, ARBs, β-blockers, aspirin, or statins	7
Nishimura 2016 [21]	Japan	Retrospective cohort study	Patients hospitalized for CVD	2419 (70.7)	57–76	1.0–1.4	> 1.4	Total death:302 1.42 (0.78–2.57); CV death:115 2.14 (0.94–4.86)	4.7	Age, sex, BMI, smoking, hemoglobin, previous MI, cerebral infarction or heart failure, dyslipidemia, DM, and hemodialysis	7
Hendriks 2016 [22]	The Netherlands	Prospective cohort study	CVD or a high risk for CVD	7542 (67)	55.6 ± 12.4	0.9–1.4	≥1.4	Total death:680 0.95 (0.67–1.34) CV death:302 1.14 (0.70–1.85)	6.9	Age, sex, smoking, DM, non-HDL-C, SBP, eGFR, and prevalent CVD	8
Velescu 2017 [23]	Spain	Prospective cohort study	General population	5679 (46.1)	55.6 ± 12.2	0.9–1.4	≥1.4	Total death:286 1.5 (0.94–2.28); CV death:57 1.8 (0.77–4.16)	6.2	Age, sex, smoking, SBP, hypertension treatment, DM, LDL, HDL, cholesterol treatment	8
Miguel 2018 [24]	Brazil	Prospective study	Hemodialysis	478 (56)	18–75	0.9–1.3	> 1.3	Total death:158 1.16 (0.60–2.26)	5.0	Age, gender, race, DM, time on dialysis, smoking, coronary disease, stroke sequelae, albumin, hemoglobin, i-PTH, ionized calcium, phosphorus, eKt/V, and CRP	7

ABI, ankle brachial index; OR, odds ratio; HR, hazard ratio; CI, confidence interval; BMI, body mass index; TC, total cholesterol; LDL, low-density lipoprotein; BP, blood pressure; DBP, diastolic blood pressure; HbA1c, glycosylated hemoglobin; CRP,C-reactive protein; hs-CRP, high-sensitivity C-reactive protein; i-PTH: intact parathyroid hormone; PA, physical activity; DM, diabetes mellitus; AF, atrial fibrillation; MI, myocardial infarction; PAD, peripheral arterial disease; CV, cardiovascular; CAD, coronary artery disease; CHF, congestive heart failure; LVEF, left ventricular ejection fraction; eGFR, estimated glomerular filtration rate; ACEIs, angiotensin-converting enzyme inhibitors; ARBs, angiotensin receptor blockers; NOS, Newcastle–Ottawa Scale.

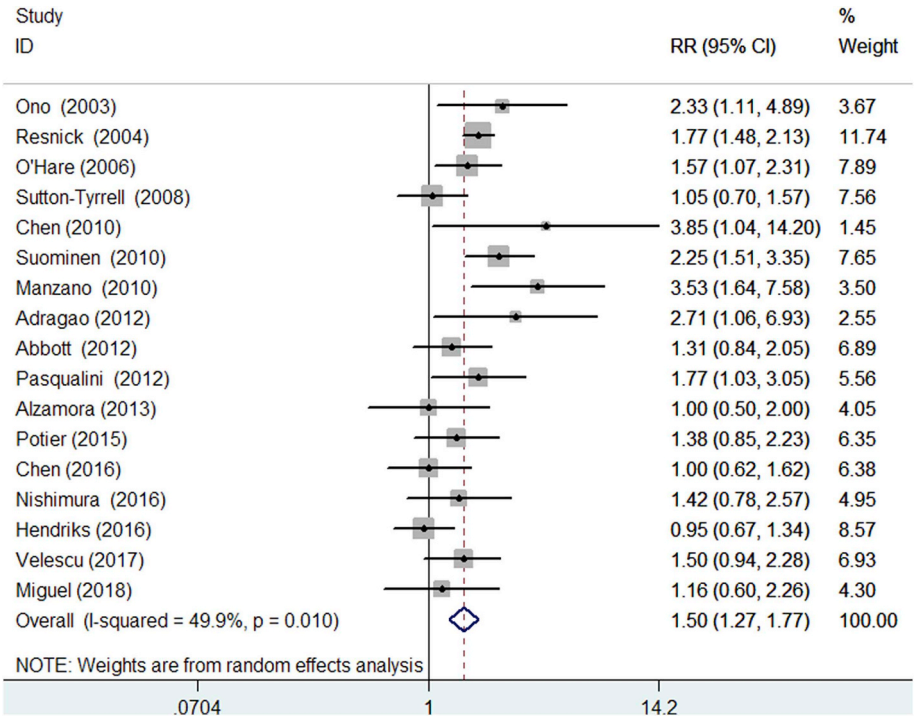

Fig. 2. Forest plots showing RR and 95% CI of all-cause mortality comparing abnormal high ankle-brachial index with reference normal ankle-brachial index.

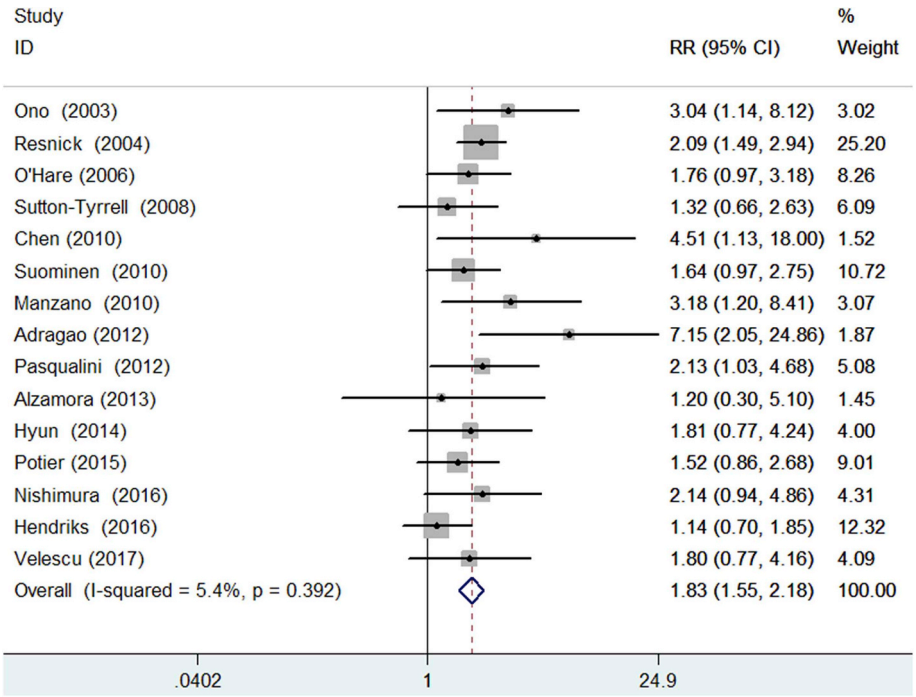

Fig. 3. Forest plots showing RR and 95% CI of cardiovascular mortality comparing abnormal high ankle-brachial index with reference normal ankle-brachial index.

should be with caution. Finally, we could not determine the optimal threshold of abnormally high ABI due to different cutoff value of high ABI used in the included studies.

4.1. Conclusions

Abnormally high ABI independently predicts all-cause mortality irrespective of the general population, CKD/hemodialysis or suspected or established cardiovascular disease patients. This meta-analysis highlighted that routine measurement of ABI could identify individuals who are at high risk of all-cause mortality. However, the association between abnormally high ABI and cardiovascular mortality should be verified in more well-designed studies. Future randomized controlled trials assessing potential benefits of treatment of high ABI may be warranted.

Table 2
Subgroup analyses.

Subgroup	No. of studies	Pooled risk ratio	95% confidence interval	Heterogeneity between studies
(A) All-cause mortality				
Sample size				
< 2000	7	2.13	1.65–2.76	$p = 0.368$; $I^2 = 7.9\%$;
> 2000	10	1.31	1.10–1.56	$p = 0.059$; $I^2 = 45.2\%$
Study type				
Prospective	14	1.47	1.21–1.78	$p = 0.010$; $I^2 = 53.0\%$
Retrospective	3	1.66	1.15–2.38	$p = 0.168$; $I^2 = 43.8\%$
Follow-up period				
< 5 years	9	1.88	1.46–2.41	$p = 0.196$; $I^2 = 27.9\%$
≥5 years	8	1.30	1.06–1.59	$p = 0.027$; $I^2 = 55.7\%$
Study population				
General population	5	1.45	1.16–1.82	$p = 0.128$; $I^2 = 44.0\%$
CKD/hemodialysis	5	1.67	1.03–2.71	$p = 0.086$; $I^2 = 51.0\%$
Suspected/established CVD	6	1.55	1.10–2.20	$p = 0.007$; $I^2 = 68.4\%$
Adjustment for lipids				
Yes	10	1.48	1.21–1.82	$p = 0.016$; $I^2 = 55.8\%$
No	7	1.57	1.14–2.16	$p = 0.076$; $I^2 = 47.5\%$
Adjustment for blood pressure				
Yes	13	1.52	1.24–1.85	$p = 0.003$; $I^2 = 59.5\%$
No	4	1.44	1.06–1.96	$p = 0.535$; $I^2 = 0.0\%$
Adjustment for smoking				
Yes	12	1.33	1.13–1.56	$p = 0.144$; $I^2 = 30.9\%$
No	5	2.16	1.61–2.90	$p = 0.281$; $I^2 = 20.9\%$
(B) Cardiovascular mortality				
Sample size				
< 2000	7	2.30	1.68–3.15	$p = 0.342$; $I^2 = 11.5\%$;
> 2000	8	1.67	1.36–2.05	$p = 0.634$; $I^2 = 0.0\%$
Study type				
Prospective	13	1.85	1.53–2.22	$p = 0.271$; $I^2 = 17.1\%$
Retrospective	2	1.77	1.14–2.75	$p = 0.592$; $I^2 = 0.0\%$
Follow-up period				
< 5 years	9	2.08	1.59–2.72	$p = 0.357$; $I^2 = 9.3\%$
≥5 years	6	1.69	1.35–2.10	$p = 0.470$; $I^2 = 0.0\%$
Study population				
General population	5	1.84	1.43–2.38	$p = 0.772$; $I^2 = 0.0\%$
CKD/hemodialysis	3	4.28	2.18–8.40	$p = 0.571$; $I^2 = 0.0\%$
Suspected/established CVD	6	1.58	1.22–2.05	$p = 0.497$; $I^2 = 0.0\%$
Adjustment for lipids				
Yes	11	1.75	1.45–2.11	$p = 0.696$; $I^2 = 0.0\%$
No	4	2.33	1.54–3.53	$p = 0.114$; $I^2 = 49.5\%$
Adjustment for blood pressure				
Yes	12	1.80	1.50–2.17	$p = 0.563$; $I^2 = 0.0\%$
No	3	2.03	1.31–3.14	$p = 0.085$; $I^2 = 59.4\%$
Adjustment for smoking				
Yes	10	1.56	1.27–1.93	$p = 0.935$; $I^2 = 0.0\%$
No	5	2.48	1.85–3.31	$p = 0.301$; $I^2 = 17.9\%$

Conflicts of interest

The authors declared they do not have anything to disclose regarding conflict of interest with respect to this manuscript.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.atherosclerosis.2018.12.028.

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