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SYSTEMATIC REVIEW

Running to Lower Resting Blood Pressure: A Systematic Review and Meta-analysis

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Abstract

Background According to previous epidemiological studies, there are pros and cons for the relationship between running regularly and changes in resting blood pressure (RBP), and the changes may depend on the form of exercise.

Objective The aims of the current systematic review were to summarize the effects of running regularly on RBP and to investigate the most efficacious form of running in reducing RBP for this purpose.

Methods The inclusion criteria were: randomized controlled trials, involving healthy adults or adults with hypertension, the exercise group only performed regular running and the control group did not exercise, and the study reported the mean resting systolic blood pressure (RSBP) and/or diastolic blood pressure (RDBP). The mean difference (MD) in RBP in each trial was defined as follows: (mean value at post-intervention in the exercise group − mean value at baseline in the exercise group) − (mean value at post-intervention in the control group − mean value at baseline in the control group) and was calculated. The weighted MD (WMD) was defined as the synthesis of all MD. A linear meta-regression analysis, exercise intensity [the percentage of maximum heart rate] (%) and total exercise time throughout the intervention (hours) were selected as explanatory variables and the MD in RBP served as the objective variable.

Results Twenty-two trials (736 subjects) were analyzed. When trials were limited to those involving healthy subjects, the WMD in RBP decreased significantly [RSBP: − 4.2 mmHg (95% confidence intervals (95% CI) − 5.9 to − 2.4); RDBP: − 2.7 mmHg (95% CI − 4.2 to − 1.1)] and did not contain significant heterogeneity (RSBP: $P = 0.67$, $I^2 = 0.0\%$; DBP: $P = 0.38$, $I^2 = 7.2\%$). When trials were limited to those involving subjects with hypertension, the WMD in RBP decreased significantly [RSBP: − 5.6 mmHg (95% CI − 9.1 to − 2.1); RDBP: − 5.2 mmHg (95% CI − 9.0 to − 1.4)] but contained significant heterogeneity (RSBP: $P = 0.01$, $I^2 = 62.2\%$; DBP: $P < 0.01$, $I^2 = 87.7$) and a meta-regression analysis showed that the percentage of maximum heart rate was significantly associated with the WMD in RSBP [slope: 0.56 (95% CI 0.21 to 0.92), intercept: − 48.76 (95% CI − 76.30 to − 21.22), $R^2 = 0.88$] and RDBP [slope: 0.45 (95% CI 0.01 to 0.87), intercept: − 38.06 (95% CI − 72.30 to − 4.08), $R^2 = 0.41$]. When trials were limited to those involving subjects with hypertension and a mean age ≥ 40 years, a meta-regression analysis showed that total exercise time throughout the intervention was significantly associated with the WMD in RDBP [slope: 0.82 (95% CI 0.54 to 1.09), intercept: − 22.90 (95% CI − 29.04 to − 16.77), $R^2 = 0.99$].

Conclusions Running regularly decreases RBP, but the changes in subjects with hypertension may differ depending on exercise intensity or total exercise time. Therefore, running regularly at moderate intensity and at a restrained volume is recommended to lower RBP in subjects with hypertension.

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Key Points

Running regularly decreases resting systolic blood pressure and diastolic blood pressure in healthy adults or adults with hypertension.

Running regularly at moderate intensity and at a restrained volume is recommended to lower resting blood pressure in adults with hypertension.

1 Introduction

An increasing number of people over 40 years of age are being found to have hypertension, which is a major risk factor for cardiovascular disease or stroke [1]. An increase in resting blood pressure (RBP) of a few mmHg has a substantial impact on worsening morbidity and mortality for those conditions [2]. Several studies have indicated that the incidence of hypertension largely depends on one's lifestyle [3] and that lifestyle modifications lower RBP [4–14]. There are several ways to alleviate hypertension [4], one of which is exercise therapy, which is less expensive than drug therapy and therefore desirable [15]. Meta-analyses of randomized controlled trials (RCTs) focusing on walking, resistance training, or aquatic exercise have indicated a significant reduction in RBP as a result of exercise therapy [8–12].

Running is performed at moderate to vigorous intensity [greater than 6 metabolic equivalents (METs)] [16] and is a popular form of exercise for adults who want to remedy their lack of physical activity [17]. Several epidemiological studies reported that running regularly was associated with circulatory and vascular indices [18–21] or the morbidity and mortality from the vascular disease [22–26]. However, findings regarding exercise intensity, exercise time, and exercise frequency for improving those indices and reducing morbidity and mortality differed among those studies, and an appropriate form of running has yet to be determined. A meta-analysis of RCTs involving interventions reported a decrease in body mass and an improvement in lipid and lipoprotein levels as a result of running regularly [27], but no meta-analysis has examined the effect of running on RBP. Meta-analyses that examined the effect of aerobic exercise reported that reductions in RBP contained significant heterogeneity; a reduction in RBP presumably depends on exercise volume or the duration of the intervention [9, 12, 13]. Therefore, changes in RBP as a result of running regularly may similarly depend on the form of exercise. The hypothesis is that there is an appropriate form of running to lower RBP.

The aims of the current systematic review were to summarize the effects of running regularly on RBP and to investigate the most efficacious form of running in reducing RBP for this purpose.

2 Methods

This systematic review with a meta-analysis was performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement [28] and registered with the International Prospective Register of Systematic Reviews (PROSPERO, registration number: CRD42018103983) [29].

2.1 Data Sources

A literature search was conducted using electronic databases: MEDLINE, EMBASE, Scopus, SPORTDiscus, CINAHL, Web of Science, and Cochrane library (Electronic Supplementary Material Appendix S1). In addition, previous systematic reviews that investigate the effect of exercise on RBP were also referred to here [8–14]. These searches were performed prior to 31 July 2019.

2.2 Study Selection

The inclusion criteria for this systematic review and meta-analysis were as follows: (1) RCTs involving subjects with a mean age of 18–65 years, healthy or with hypertension but no chronic conditions, (2) RCTs in which the exercise group only performed regular running (except for combinations of running and walking) and the control group did not exercise at all; (3) RCTs in which neither group received any other intervention (e.g. improved diet or a change in lifestyle); (4) RCTs in which intervention lasted four weeks or longer; and (v) RCTs reporting the mean resting systolic blood pressure (RSBP) and/or diastolic blood pressure (RDBP) and its standard deviation (SD) or standard error (SE) at baseline and post-intervention for the exercise and the control groups.

During the first screening, articles were identified by title and abstract. If the trial included an intervention involving running and reported RBP, the full text of the article was obtained. The identified trials were reviewed by both authors to determine whether or not the trial should be included in this systematic review.

2.3 Data Extraction

The Cochrane data collection form for intervention review (RCTs only) was used to extract data [30], and both authors independently extracted data and details from the trials for the meta-analysis as follows: mean RSBP, mean RDBP data, and their respective SDs as primary outcomes; mean body mass index (BMI) in kg/m^2, mean resting heart rate (HR) in beat/min, mean maximal oxygen consumption ($\dot{V}O_{2max}$) in mL/kg/min, and their respective SDs as secondary outcomes; and the number of subjects and exercise intensity, exercise time [defined as the total exercise time per session (min/session)], exercise frequency [defined as the number of exercise sessions per week (sessions/week)], and the duration of intervention (weeks) as details of the intervention. Total exercise time (hours) was defined as the total exercise time throughout the intervention and calculated as the exercise time × exercise frequency × duration of intervention.

2.4 Assessing the Risk of Bias

Both authors used the Cochrane Collaboration tool, which consists of six domains (random sequence generation, allocation concealment, blinding, incomplete outcome data, selective reporting, and other risk), to assess the risk of bias in each trial [31]. Each domain was ranked in one of three categories: low risk, unclear risk, or high risk. Since the current review involves an exercise intervention, subjects cannot be blinded to group assignment. [9, 11, 13]. Therefore, this systematic review did not consider such blinding. In addition, trials that measured blood pressure using an automated device were assessed as having blinded the recorder (to the group that subjects belonged to).

2.5 Statistical Analyses

All meta-analyses were performed using the Comprehensive Meta-Analysis software program (Version 2.2; Biostat, Inc., Englewood, NJ).

2.5.1 Data Synthesis

The RBP and secondary outcomes at baseline were expressed as the mean ± SD weighted by the number of subjects. The mean difference (MD) in RBP and secondary outcomes in each trial was defined as follows: (mean value at post-intervention in the exercise group − mean value at baseline in the exercise group) − (mean value at post-intervention in the control group − mean value at baseline in the control group) and was calculated. The weighted MD (WMD) was defined as the synthesis of all MD, and the MD in each trial was weighted by the inverse squared SE of differences from the baseline to assessment post-intervention. In this meta-analysis, the WMD was calculated using a method of moment for random-effects model based on the DerSimonian–Laird approach [32]. This approach takes into account within-study and between-study variances as opposed to the fixed-effect model, which ignores the between-study variance and could erroneously yield positive results [32]. The correlation coefficient between the baseline and post-intervention assessment was assumed to be 0.50 [33]. The MD and WMD were expressed with a 95% confidence interval (CI). These calculations were performed individually after categorizing trials as those involving healthy subjects and subjects with hypertension.

Subgroup analyses of the WMD in RBP were limited to trials involving subjects with a mean age ≥ 40 years. In addition, a sensitivity analysis was used to evaluate the influence of the risk of bias [31]. Trials falling into one or more domains of a high risk of bias were excluded, and the WMD in RBP was then calculated.

The heterogeneity of the WMD as a result of variations among trials was assessed using Cochran's Q statistic and the I^2 statistic. In the statistical test, a P value < 0.05 was considered to indicate statistically significant heterogeneity, and the degree of heterogeneity was assessed in 3 grades: low risk ($I^2 < 25\%$), moderate risk (I^2: 25–75%), or high risk ($I^2 > 75\%$) [34].

The current review and meta-analysis performed a simple linear regression analysis in order to examine the relationship between several factors (subject characteristics or the form of running) and changes in RBP. A random-effect simple linear meta-regression model (method of moment approach) was used for the analysis. First, in the sensitivity analyses, age was selected as an explanatory variable, and the MD in RBP served as the objective variable. Second, the percentage of maximum HR (% HR_{max}) as exercise intensity [if trials indicated the percentage of $\dot{V}O_{2max}$ (% $\dot{V}O_{2max}$), the value was converted to the % HR_{max} using the equation of Londeree and Ames] [35] and total exercise time (hours) were selected as explanatory variables, and the MD in RBP served as the objective variable. The slope and intercept of the meta-regression equation were calculated, and then the adjusted R^2 (the proportion of between study variance explained by covariates) was calculated [36]. The slope and intercept were expressed with a 95% CI (and P values). Analyses were performed individually after categorizing trials into those involving healthy subjects and those involving subjects with hypertension. In addition, the explanatory variables % HR_{max} and total exercise time were included in an additional analysis of trials involving subjects with a mean age ≥ 40 years.

Funnel plots were created with the MD in RBP (x-axis) and the SE (y-axis) to assess publication bias, and this meta-analysis used two statistical methods to assess the influence of bias. First, Egger's regression test was used to evaluate the asymmetry of funnel plots [37]. The results of Egger's regression test were expressed as the 95% CI. If the CI did not cross zero, the funnel plot was deemed to have significant asymmetry. Second, the trim and fill method of Duval and Tweedie was used to estimate the number of missing trials and coordinate where they were located on a funnel plot [38]. If the results suggested that trials were missing, then the WMD in RBP was adjusted by the addition of coordinates. The results were expressed as the WMD in light of the effect of these trials and the 95% CI.

3 Results

3.1 Study Characteristics

Figure 1 shows the steps in the search process. As a result of the literature search and screening of articles, 22 trials reported in 17 articles and involving 736 subjects (exercise group: $n=409$; control group: $n=327$) [39–55] were ultimately analyzed. Table 1 shows a general description of the RCTs. Twenty trials [39–43, 45–55] reported the number of subjects by sex, and trials involved 422 males (59.2%) and 291 females (40.8%). All trials reported the mean age, which ranged from 21 to 49 years. All trials used a parallel design and were published in peer-reviewed journals.

Table 1 also shows the details of the exercise intervention. Twenty trials [39, 40, 42–52, 54, 55] expressed exercise intensity as the % HR_{max}. All trials had a set exercise time and exercise frequency. When trials were limited to those involving healthy subjects [39, 41, 43, 48, 50–55], exercise intensity ranged from 70 to 85% and the total exercise time ranged from 6 to 126 h. When trials were limited to those involving subjects with hypertension [40, 42, 44–47, 49], exercise intensity ranged from 66 to 88% and the total exercise time ranged from 15 to 48 h. When trials were limited to those involving healthy subjects and a mean age ≥ 40 years [43, 51, 53, 54], exercise intensity ranged from 70 to 82% and the total exercise time ranged from 18 to 126 h. When trials were limited to those involving subjects with hypertension and a mean age ≥ 40 years [42, 44–47], exercise intensity ranged from 66 to 88% and the total exercise time ranged from 15 to 28 h.

Figure 2 and Electronic Supplementary Material Table S1 show the results for the assessed risk of bias. The Cochrane Collaboration tool indicated a low risk of bias or an unclear risk of bias in random sequence generation, allocation concealment, blinding, selective reporting, and other risks but one trial [41] had a high risk of bias because of incomplete outcome data.

3.2 Data Synthesis

Figures 3 and 4 show the results of baseline and forest plots of the MD from each trial and the WMD in RSBP and RDBP, respectively. When trials were limited to those involving healthy subjects, the WMD in RSBP and RDBP decreased significantly and did not contain significant heterogeneity (low risk). When trials were limited to those involving subjects with hypertension, the WMD in RSBP and RDBP decreased significantly but contained significant heterogeneity (moderate risk and high risk, respectively). When trials were limited to those involving healthy subjects or subjects with hypertension, resting HR (a secondary outcome) decreased significantly and $\dot{V}O_{2max}$ (another secondary outcome) increased significantly. No significant heterogeneity in BMI, resting HR, or $\dot{V}O_{2max}$ was noted (Electronic Supplementary Material Table S2).

Table 2 shows the results of the subgroup and sensitivity analyses. When trials were limited to those involving healthy subjects and a mean age ≥ 40 years [43, 50–54], the WMDs in RSBP and RDBP decreased significantly and did not contain significant heterogeneity (low risk). However, when trials were limited to those involving subjects with hypertension and a mean age ≥ 40 years [42, 44–47], the WMDs in RSBP and RDBP decreased significantly but contained

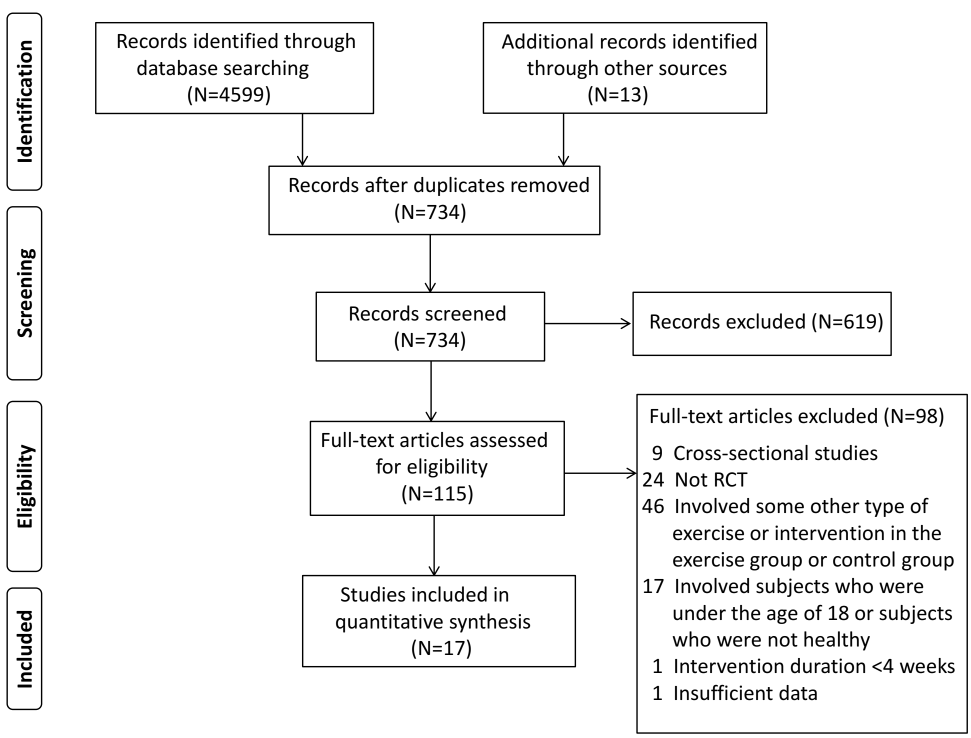

Fig. 1 PRISMA flow diagram regarding article selection for meta-analysis. *RCT* randomized controlled trial

Table 1 Characteristics of the analyzed RCTs

Study	Subject with hypertension	*n*	Female (%)	Mean age (year)	Exercise intervention	Duration of intervention (weeks)
Mathur et al. [39], Nigeria	No	20	0	24 ± 3	85% HR_{max}, 5–10 min (1.6 km), 3 sessions/week	12
Mathur et al. [39], Nigeria	No	20	0	24 ± 3	85% HR_{max}, 12–18 min (3.2 km), 3 sessions/week	12
Mathur et al. [39], Nigeria	No	20	0	24 ± 3	85% HR_{max}, 18–25 min (4.8 km), 3 sessions/week	12
Duncan et al. [40], USA	Yes	56	0	30	70–80% HR_{max}, 60 min, 3 sessions/week	16
Suter et al. [41], Switzerland	No	61	0	38 ± 8	85% AT, 30–45 min, 2-6 sessions/week (at least 120 min per week)	16
Blumenthal et al. [42], USA	Yes	61	36	45 ± 8	70% $\dot{V}O_{2max}$, 35 min, 3 sessions/week	16
Albright et al. [43], USA	No	43	0	49 ± 6	65–77% HR_{max}, 47 min, 5 sessions/week	24
Albright et al. [43], USA	No	40	100	47 ± 5	65–77% HR_{max}, 54 min, 5 sessions/week	24
Rogers et al. [44], USA	Yes	11	NR	43 ± 7	40–50% $\dot{V}O_{2max}$, 45 min, 3 sessions/week	12
Rogers et al. [44], USA	Yes	12	NR	40 ± 6	70–80% $\dot{V}O_{2max}$, 45 min, 3 sessions/week	12
Tsai et al. [45], Taiwan	Yes	23	48	48 ± 8	60–70% HR_{max}, 30 min, 3 sessions/week	12
Tsai et al. [46], Taiwan	Yes	42	45	41 ± 9	60–70% HR_{max}, 30 min, 3 sessions/week	12
Tsai et al. [47], Taiwan	Yes	102	54	49 ± 7	60–70% HR_{max}, 30 min, 3 sessions/week	10
Krustrup et al. [48], Denmark	No	20	0	31 ± 6	82% HR_{max}, 60 min, 2-3 sessions/week	12
Knoepfli-Lenzin et al. [49], Switzerland	Yes	32	0	37 ± 5	79.4% HR_{max}, 58 min, 2.4 sessions/week	12
Krustrup et al. [50], Denmark	No	15	100	40 ± 8	81–82% HR_{max}, 60 min, 2 sessions/week	64
Amin-Shokravi et al. [51], Iran	No	40	100	46 ± 2	70–80% HR_{max}, 30 min, 3 sessions/week	12
Beck et al. [52], USA	No	28	32	21 ± 3	Walking, 65% HR_{max}, 3 min and running, 85% HR_{max}, 2 min, total 45 min (interval training), 3 sessions/week	8
Foulds et al. [53], Canada	No	40	58	40 ± 14	30 min, 3 sessions/week	13
Hur et al. [54], Republic of Korea	No	24	100	48 ± 2	60–70% HR_{max}, 40 min, 3 sessions/week	40
Hur et al. [54], Republic of Korea	No	22	100	47 ± 2	60–70% HR_{max}, 40 min, 3 sessions/week	40
Patterson et al. [55], UK	No	22	100	34 ± 7	75% HR_{max}, 50 min, 3 sessions/week	8

AT anaerobic threshold, *% HR_{max}* percentage of maximum heart rate, *% HRR* percentage of heart rate reserve, *LT* lactate threshold, *n* number of subjects, *NR* not reported, *RCT* randomized controlled trial, *RPE* rate of perceived exertion, *% $\dot{V}O_{2max}$* percentage of maximal oxygen uptake, *$\dot{V}O_{2peak}$* peak oxygen uptake

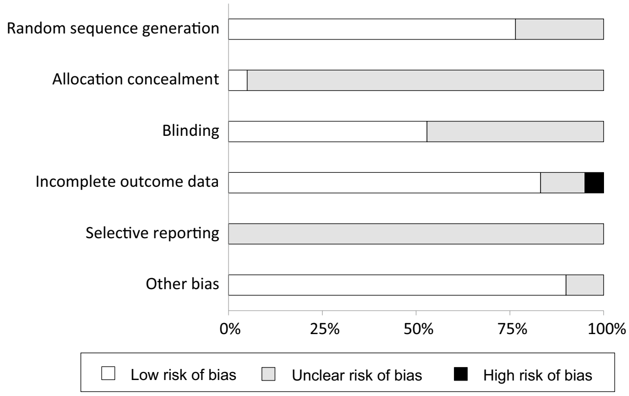

Fig. 2 Overall results for risk of bias

significant heterogeneity (moderate risk). In addition, when one trial [41] that had a high risk of bias was excluded, the sensitivity analysis indicated that the WMD in RSBP and RDBP decreased significantly and did not contain significant heterogeneity (low risk).

Table 3 shows the results of a meta-regression analysis of the relationship between the form of running (an explanatory variable) and the WMD in RBP (the objective variable). When trials were limited to those involving healthy subjects, all explanatory variables were not significantly associated with the MD in RSBP and RDBP. When trials were limited to those involving subjects with hypertension, the % HR_{max} was significantly associated with the MD in RSBP and RDBP [$y = 0.56x - 48.76$ (Eq. 1) and $y = 0.45x - 38.06$ (Eq. 2), respectively, where y was the MD in RBP and x was % HR_{max}, Electronic Supplementary Material Figure S1 and S2]. When trials were limited to those involving subjects with hypertension and a mean age ≥ 40 years, the % HR_{max} was significantly associated with the MD in RSBP and RDBP [$y = 0.57x - 48.61$ (Eq. 3) and $y = 0.50x - 42.61$ (Eq. 4), respectively, where y was the MD in RBP and x was % HR_{max}, Electronic Supplementary Material Figure S3 and S4]. In addition, when trials were limited to those involving subjects with hypertension and a mean age ≥ 40 years, total exercise time was significantly associated with the MD in RDBP [$y = 0.82x - 22.90$ (Eq. 5), where y was the MD in RDBP and x was total exercise time (min), Electronic Supplementary Material Figure S5].

Egger's regression test revealed no significant asymmetry of the funnel plots for RSBP and RDBP when trials were

Study	n	Baseline	MD (95% CI)
Healthy			
Mathur et al., 1984a [39]	20	126.8 ± 10.3	−2.2 (−7.8 to 3.4)
Mathur et al., 1984b [39]	20	127.6 ± 10.3	−5.4 (−11.6 to 0.8)
Mathur et al., 1984c [39]	20	127.2 ± 10.3	−6.6 (−13.3 to 0.1)
Suter et al., 1990 [41]	61	133.3 ± 10.4	2.5 (−5.7 to 10.7)
Albright et al., 1992a [43]	43	118.5 ± 9.6	−3.0 (−10.4 to 4.4)
Albright et al., 1992b [43]	40	105.4 ± 10.9	1.0 (−6.9 to 8.9)
Krustrup et al., 2009 [48]	20	130.0 ± 9.2	−6.0 (−14.8 to 2.8)
Krustrup et al., 2010 [50]	15	109.5 ± 10.2	0.0 (−10.7 to 10.7)
Amin-Shokravi et al., 2011 [51]	40	118.4 ± 8.3	−5.2 (−8.4 to −1.9)
Beck et al., 2013 [52]	28	130.9 ± 11.9	−12.0 (−21.0 to −3.0)
Foulds et al., 2014 [53]	24	110.7 ± 10.2	−4.8 (−16.4 to 6.8)
Hur et al., 2014a [54]	24	137.1 ± 10.1	−2.5 (−8.1 to 3.1)
Hur et al., 2014b [54]	22	130.1 ± 12.5	−7.2 (−16.3 to 1.9)
Patterson et al., 2017 [55]	20	120.2 ± 8.6	−5.0 (−13.9 to 3.9)
Pooled	**397**	**123.3 ± 10.2**	**−4.2 (−5.9 to −2.4)**
(Heterogeneity)			**Q=10.3, P=0.67; I^2=0.0%**
Hypertension			
Duncan et al., 1985 [40]	56	146.0 ± 6.1	−6.2 (−10.5 to −1.9)
Blumenthal et al., 1991 [42]	61	141.4 ± 10.2	1.0 (−4.3 to 6.3)
Rogers et al., 1996a [44]	11	140.0 ± 9.8	−14.0 (−22.3 to −5.7)
Rogers et al., 1996b [44]	12	138.8 ± 9.5	−3.0 (−9.8 to 3.8)
Tsai et al., 2002 [45]	23	141.4 ± 12.2	−10.0 (−19.5 to −0.5)
Tsai et al., 2002 [46]	42	135.9 ± 9.8	−8.0 (−15.4 to −0.6)
Tsai et al., 2004 [47]	102	142.8 ± 11.3	−9.5 (−15.0 to −4.0)
Knoepfli-Lenzin et al., [49]	32	134.1 ± 8.9	0.0 (−4.8 to 4.8)
Pooled	**339**	**141.1 ± 9.9**	**−5.6 (−9.1 to −2.1)**
(Heterogeneity)			**Q=18.5, P=0.01; I^2=62.2%**

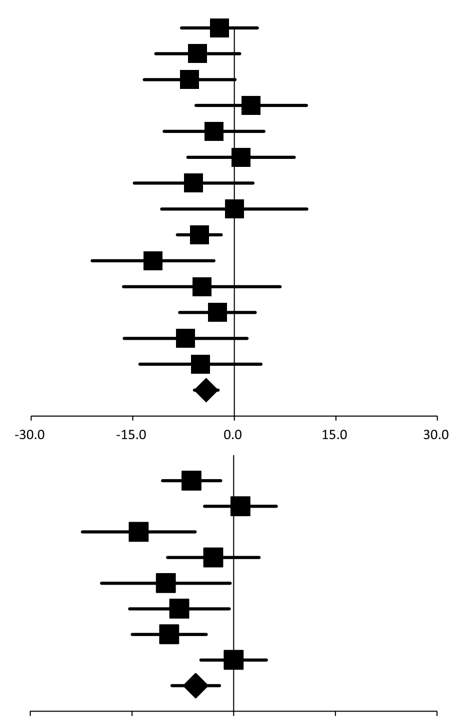

Fig. 3 Baseline mean RSBP and forest plot for the MD in RSBP. Baseline mean RSBP was expressed as the mean ± standard deviation weighted by the number of subjects. Each trial is presented by black squares (MD) and width (95% CI). The WMD (i.e., overall MD) is represented by black rhombuses (WMD) and widths (95% CI). *CI* confidence interval, *MD* mean difference, *RSBP* resting systolic blood pressure, *WMD* weighted mean difference

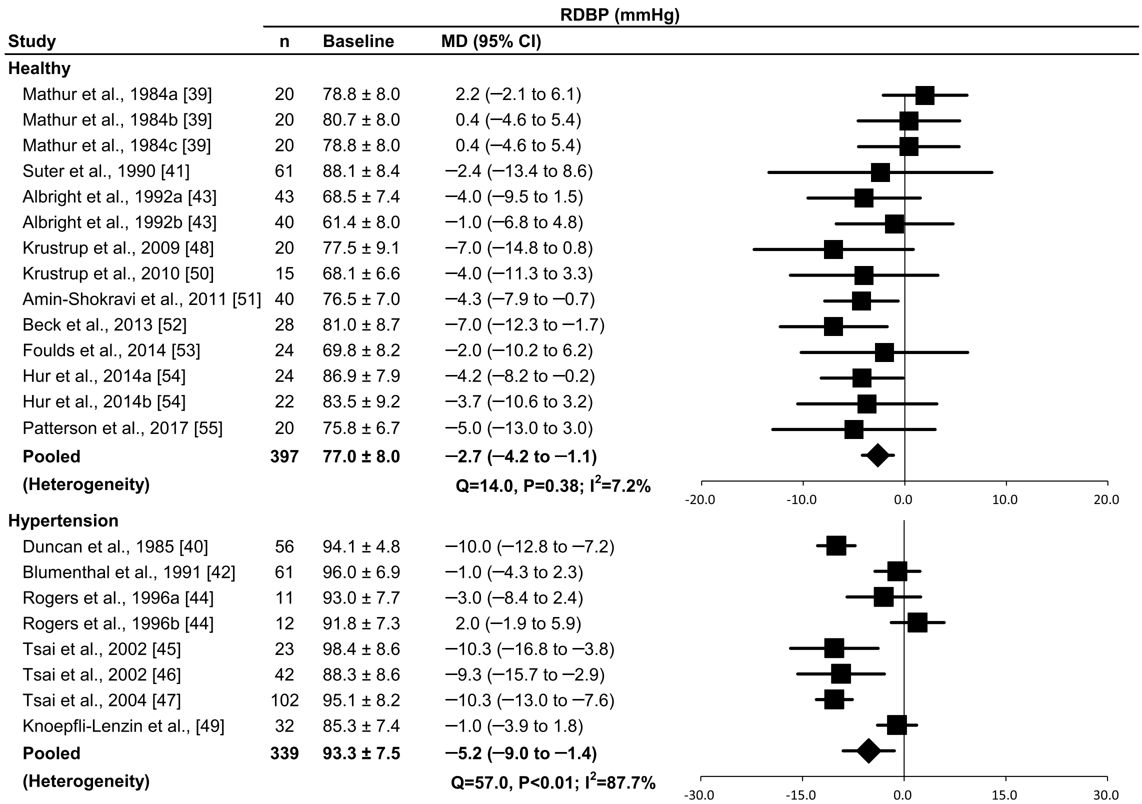

Fig. 4 Baseline mean RDBP and forest plot for the MD in RDBP. Baseline mean RSBP was expressed as the mean ± standard deviation weighted by the number of subjects. Each trial is presented by black squares (MD) and width (95% CI). The WMD (i.e., overall MD) is represented by black rhombuses (WMD) and widths (95% CI). *CI* confidence interval, *RDBP* resting diastolic blood pressure, *MD* mean difference, *WMD* weighted mean difference

Table 2 Results of subgroup and sensitivity analyses

Categories	Trials (*n*)	RSBP				RDBP			
		Baseline, mmHg	WMD (95% CI), mmHg	*Q*	I^2 %	Baseline, mmHg	WMD (95% CI), mmHg	*Q*	I^2 %
Mean age ≥ 40 years									
Healthy	7 (208)	117.8 ± 10.1	− 3.9 (− 6.2 to − 1.6)	3.4	0.0	72.5 ± 7.8	− 3.6 (− 5.6 to − 1.7)	1.2	0.0
Hypertension	6 (251)	140.9 ± 10.7	− 6.8 (− 11.4 to − 2.1)	13.6*	63.2	94.2 ± 8.0	− 5.1 (− 9.9 to − 0.4)	37.6*	86.7
Not included a high risk of bias									
Healthy	13 (336)	121.4 ± 10.2	− 4.5 (− 6.3 to − 2.7)	7.6	0.0	74.9 ± 7.9	− 2.7 (− 4.3 to − 1.1)	14.0	14.4

Baseline RSBP and RDBP are expressed as the mean ± standard deviation weighted by the number of subjects

CI confidence interval, *RSBP* resting systolic blood pressure, *RDBP* resting diastolic blood pressure, *n* number of subjects, *WMD* weighted mean difference

*Significant heterogeneity ($P < 0.05$)

limited to those involving healthy subjects, healthy subjects with a mean age ≥ 40 years, subjects with hypertension, or subjects with hypertension and a mean age ≥ 40 years (Electronic Supplementary Material Table S3). When trials were limited to those involving healthy subjects or subjects with hypertension and a mean age ≥ 40 years, Duval and Tweedie's trim and fill suggested that there were no missing data for RSBP. In addition, when trials were limited to those involving healthy subjects and a mean age ≥ 40 years, Duval and Tweedie's trim and fill suggested that there were no missing data for RDBP. Some data for the other variables were presumably missing. However, after adjusting for the effects of those missing trials, none of the WMDs changed significantly (Electronic Supplementary Material Table S3).

Table 3 Relationships between the WMD in RBP and variables using a meta-regression analysis

Explanatory variables	Trials (n)	Slope (95% CI)	P	Intercept (95% CI)	P	Adjusted R^2
RSBP						
Healthy						
Age (years)	14 (397)	0.08 (−0.09 to 0.25)	0.37	−7.18 (−13.99 to −0.37)	0.04	0.13
% HR_{max}	12 (312)	−0.14 (−0.51 to 0.23)	0.45	6.71 (−22.6 to 36.03)	0.45	0.00
% HR_{max} (mean age ≥ 40 years)	6 (176)	−0.07 (−0.63 to 0.48)	0.80	1.62 (−41.27 to 44.52)	0.94	0.00
Total exercise time (h)	14 (397)	0.04 (−0.01 to 0.09)	0.10	−5.76 (−8.34 to −3.18)	< 0.01	0.29
Total exercise time (h) (mean age ≥ 40 years)	7 (200)	0.04 (−0.02 to 0.10)	0.15	−6.10 (−9.97 to −2.24)	< 0.01	0.00
Hypertension						
Age (years)	8 (339)	−0.21 (−0.84 to 0.43)	0.53	2.77 (−23.58 to 29.12)	0.84	0.00
% HR_{max}	8 (339)	0.56 (0.21 to 0.92)	< 0.01	−48.76 (−76.30 to −21.22)	< 0.01	0.88
% HR_{max} (mean age ≥ 40 years)	6 (251)	0.57 (0.22 to 0.90)	< 0.01	−48.61 (−75.19 to −22.03)	< 0.01	0.95
Total exercise time (h)	8 (339)	0.12 (−0.26 to 0.50)	0.55	−8.82 (−19.79 to 2.16)	0.11	0.00
Total exercise time (h) (mean age ≥ 40 years)	6 (251)	0.48 (−0.29 to 1.24)	0.22	−17.23 (−34.81 to −0.35)	0.06	0.29
RDBP						
Healthy						
Age (years)	14 (397)	−0.11 (−0.24 to 0.02)	0.11	1.31 (−3.75 to 6.37)	0.61	0.06
% HR_{max}	12 (312)	0.21 (−0.09 to 0.50)	0.17	−19.33 (−42.97 to 4.31)	0.11	0.32
% HR_{max} (mean age ≥ 40 years)	6 (176)	0.01 (−0.44 to 0.46)	0.97	−4.46 (−36.69 to 29.77)	0.80	0.00
Total exercise time (h)	14 (397)	−0.02 (−0.06 to 0.02)	0.37	−1.87 (−4.16 to 0.43)	0.11	0.00
Total exercise time (h) (mean age ≥ 40 years)	7 (200)	0.01 (−0.04 to 0.06)	0.74	−4.22 (−8.20 to −0.24)	0.04	0.00
Hypertension						
Age (years)	8 (339)	−0.08 (−0.80 to 0.65)	0.84	−2.08 (−32.41 to 28.24)	0.84	0.00
% HR_{max}	8 (339)	0.45 (0.01 to 0.89)	0.04	−38.06 (−72.30 to −4.08)	< 0.01	0.41
% HR_{max} (Mean age ≥ 40 years)	6 (251)	0.50 (0.15 to 0.85)	< 0.01	−42.61 (−69.12 to −16.11)	< 0.01	0.76
Total exercise time (h)	8 (339)	0.05 (−0.39 to 0.48)	0.83	−6.53 (−18.85 to 5.80)	0.30	0.00
Total exercise time (h) (mean age ≥ 40 years)	6 (251)	0.82 (0.54 to 1.09)	< 0.01	−22.90 (−29.04 to −16.77)	< 0.01	0.99

Total exercise time is defined as time (min) × frequency (sessions per week) × duration (weeks)

CI confidence interval, *RDBP* resting diastolic blood pressure, *% HR_{max}* percentage of maximum heart rate, *n* number of subjects, *RSBP* resting systolic blood pressure, *WMD* weighted mean difference

4 Discussion

The current review evaluated the effect of running regularly on RBP using meta-analyses, and findings indicated that RSBP, RDBP, and resting HR decreased and $\dot{V}O_{2max}$ increased. However, when trials were limited to those involving subjects with hypertension, changes in RSBP and RDBP were heterogeneous. The hypothesis was that this heterogeneity was due to the form of running (i.e. the exercise volume). Accordingly, the relationship between the form of running and changes in RBP was analyzed. When trials were limited to those involving subjects with hypertension, results indicated that RSBP and RDBP were associated with the exercise intensity (% HR_{max}). In addition, when trials were limited to those involving subjects with hypertension and a mean age ≥ 40 years, results indicated that RDBP was associated with the total exercise time throughout the intervention. Therefore, changes in RBP may differ depending on the form of running performed by subjects with hypertension.

4.1 Comparison with Other Studies

Several meta-analyses of RCTs reported a decrease in RBP as a result of regular aerobic exercise and RSBP of approximately −3 mmHg and RDBP of approximately −2 mmHg [8–14]. In addition, some of these results contained significant heterogeneity while others did not [8–10, 12, 13]. The current review found that running regularly decreased RSBP by approximately 5 mmHg and RDBP by approximately

4 mmHg. In addition, this review found that these effects had a moderate to high risk of heterogeneity in subjects with hypertension but had a low risk of heterogeneity in healthy subjects, so a difference in heterogeneity was apparent depending on whether or not subjects had hypertension. This heterogeneity may have been because of differences in the exercise intensity or total exercise time among trials. In general, exercise at a moderate intensity means 64–76% HR_{max}, and exercise at a vigorous intensity means 77–93% HR_{max} [56]. According to meta-regression equations used in the current review, RSBP and RDBP are estimated to decrease by approximately 12 mmHg and 10 mmHg, respectively, when running at 64% HR_{max} [i.e. the value of 64 was substituted for x in Eqs. (1)–(4)] and by approximately 5 mmHg and 4 mmHg, respectively, when running at 77% HR_{max} [i.e. the value of 77 was substituted for x in Eqs. (1)–(4)]. Therefore, the current review found that running at a moderate intensity has a beneficial effect by decreasing RBP more so than running at vigorous intensity, and this is especially true in adults with hypertension. In addition, as mentioned earlier, when trials were limited to those subjects with hypertension and a mean age $\geq$ 40 years, the total exercise time ranged from 15 to 28 h. When these total exercise times were used in the meta-regression analysis, the slopes of the meta-regression equations [Eq. (5)] expressed the relationship between the total exercise time and change in RDBP. Previous systematic reviews and meta-analyses involving East Asians reported that exercise intensity or total exercise time was not associated with RBP as a result of regular aerobic exercise, but those reviews and meta-analyses also involved subjects with lifestyle-related diseases and they did not perform a subgroup analysis of healthy subjects and subjects with hypertension [13]. Similarly, no systematic reviews and meta-analyses distinguished subjects with or without disease nor did they investigate the relationship between the form of exercise and changes in RBP [8–12, 14]. When the current review excluded trials involving subjects with chronic diseases such as lifestyle-related diseases (not including hypertension), only trials involving subjects with hypertension contained heterogeneity, as mentioned earlier, and these trials noted a relationship between RBP and the form of exercise. Therefore, having a condition or not and the form of exercise are considered to be factors influencing changes in RBP, and a strength of the current review is probably that it investigated the effects of exercise categorizing RCTs into those involving subjects with or without hypertension. Since several epidemiological studies have noted a relationship between the form of exercise and changes in RBP [18, 19, 22] but few RCTs or meta-analyses have noted such a relationship [57], future studies should explore that relationship.

4.2 Mechanisms

One proposed mechanism for hypertension is that oxidative stress impairs endothelium-dependent vasodilation, leading to the development of hypertension [58]. In addition, endurance exercise at vigorous intensity over a prolonged period presumably enhances the response to oxidative stress [59, 60]. Therefore, the reasons why reductions in RBP depended on the exercise intensity in the current review presumably involve oxidative stress. However, none of the trials analyzed in our study evaluated indices of oxidative stress, and one trial evaluated indices related to vasodilation [52]. Another mechanism by which RBP changes as a result of exercise may involve changes in catecholamines [61], but only one trial analyzed in the current review examined those changes [40]. Thus, the effects of running at vigorous intensity on RBP involve complex mechanisms, and future studies should explore those mechanisms.

4.3 Limitations

Most of the trials examined in this systematic review and meta-analysis involved running at moderate or vigorous intensity (66% HR_{max} or greater), so the findings may not have provided sufficient evidence of the effects of running at light intensity for a long time or at a high frequency on RBP. Therefore, future studies should perform RCTs involving such forms of running.

5 Conclusions

The results of this review indicated that running regularly decreases RSBP and RDBP, but this effect likely depends on the exercise intensity and total exercise time in adults with hypertension. Therefore, running regularly at a moderate intensity and at a restrained volume is recommended in order to lower RBP.

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Compliance with Ethical Standards

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