

THE EFFECT OF RAMADAN FASTING TO BLOOD PRESSURE IN HYPERTENSIVE PATIENTS: A META-ANALYSIS

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ABSTRACT

Ramadan fasting is a type of time-restricted eating and drinking. Previously, a systematic review drew inconclusive effect of Ramadan fasting on blood pressure in hypertensive individuals. Therefore, this meta-analysis aims to evaluate Ramadan fasting effects on blood pressure in hypertensive individuals. This literature search was conducted in PubMed and Google Scholar. All studies assessing the effect of Ramadan fasting on blood pressure in hypertensive patients were included. Statistical analysis was performed in Review Manager 5.4. A total of 7 studies with 260 patients were analyzed. The male proportion and mean age varied from 41% to 88% and 37.5 years to 60 years, accordingly. Four studies measured blood pressure using the ambulatory method. Ramadan fasting significantly reduces systolic blood pressure (SMD=-0.77, 95%CI [-1.18—-0.36], p=0.0002) and diastolic blood pressure (SMD=-0.79, 95%CI [-1.35—-0.24], p=0.005) in hypertensive patients. Both analyses demonstrated high heterogeneity, yet the results persisted after sensitivity analysis. Publication bias was detected. Ramadan fasting reduces blood pressure among hypertensive patients. However, further and larger studies are required to justify this result.

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INTRODUCTION

Hypertension (HT) is a major burden worldwide. According to WHO (2019), HT affects an estimated 1.13 billion individuals worldwide, which less than 20% of them are under control.¹ Ironically, HT is considered as one of the strongest risk factors of majority cardiovascular disease.² Lifestyle modification is imperative in managing hypertensive patients. In fact, a higher prevalence of good lifestyle was recorded in individuals with controlled HT.³ Intermittent fasting is a form of time-limited eating which

proved to lower blood pressure.⁴ One type of intermittent fasting is Ramadan fasting (RF).

RF is mandatory for Muslims during the holy month of Ramadan. The fast starts at dawn and ends at *Maghrib*, which halts eating, drinking, smoking, or sexual activity. This unique intermittent fasting pattern significantly impacts individuals' eating and sleeping habits, along with their nutritional status.⁵ Subsequently, one prospective observational study demonstrated RF significantly reduced 10-years coronary heart disease score along with its risk factors, such as lipids profile, systolic blood pressure,

body mass index, and waist circumference.⁶ Previous systematic review drew inconclusive outcomes of RF towards blood pressure in patients with HT.⁷ Therefore, the current meta-analysis aims to evaluate the effect of RF on blood pressure (BP) in hypertensive patients.

MATERIALS AND METHODS

Study Design and Search Strategy

Current systematic review and meta-analysis was performed based on Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines.⁸ We searched respective articles in two online databases (PubMed and Google Scholar) using keywords such as “Ramadan”; “Ramadan fasting”; “Blood pressure”; “Hypertension”; and its related synonym. The search was conducted on April 2021. Additionally, we also included studies from preliminary search or reference lists of included or excluded articles to identify any additional articles. Two authors independently screened articles by title and abstracts after duplicates removal.

Subsequently, accessible full-text articles were then evaluated based on inclusion and exclusion criteria. All studies assessing the effect of Ramadan fasting on blood pressure in hypertensive patients were included in this study. Definition of pre-fasting and post-fasting BP was based on BP measurement during 1 to 10 days before and after Ramadan fasting, accordingly. Studies that were (1) review, commentary, or letter to the editor; (2) not published in English; or (3) incomplete data were excluded for further analysis.

Data Extraction and Outcome

Data regarding authors, year of publication, study design, location, sample size, participants demographic, case definition, method of BP measurements, pre-fasting BP, and post-fasting BP were collected and stored in a dedicated online spreadsheet. Outcomes for this meta-analysis were systolic BP (SBP) and diastolic BP (DBP) during the pre-fasting and post-fasting periods.

Quality and Publication Bias Assessment

The methodological quality of each included study was evaluated using the Newcastle-Ottawa Scale which was composed of three domains, selection, comparability, and outcome. A Star-scoring system was used for each domain and the final evaluation was presented as good, fair, and poor quality. Meanwhile, a visual funnel plot assessment was used to detect any publication bias among included studies.

Statistical Analysis

All statistical analysis was conducted by Review Manager 5.4. Continuous data were presented as standardized mean difference (SMD) and 95% confidence interval (95%CI). SMD of 0.2 was considered as small effect; SMD of 0.5 as medium effect; and SMD of 0.8 as large effect. A fixed-effects model was used if the heterogeneity is less significant ($I^2 \leq 50\%$), otherwise, a random-effects model was used. Additionally, leave-one-out sensitivity analysis was carried out to detect the heterogeneity culprit. All p-value ≤ 0.05 was considered statistically significant, except heterogeneity result ($p \leq 0.10$).

RESULTS

Study Selection

A total of 458 studies were collected for duplication checking. Forty-nine studies were excluded due to study duplication, leaving 409 studies for further steps. First screening removed 392 studies with irrelevant titles or abstracts, along with 3

studies with the inaccessible full-text article. Eligibility assessment eliminated 7 studies. One study was a review; 2 studies indicate a partly similar result in a different publication; 3 studies measured BP in inappropriate time; and 1 study did not report the complete result. Finally, a total of 7 studies were included in qualitative and quantitative analysis. The PRISMA flowchart is presented in Figure 1.

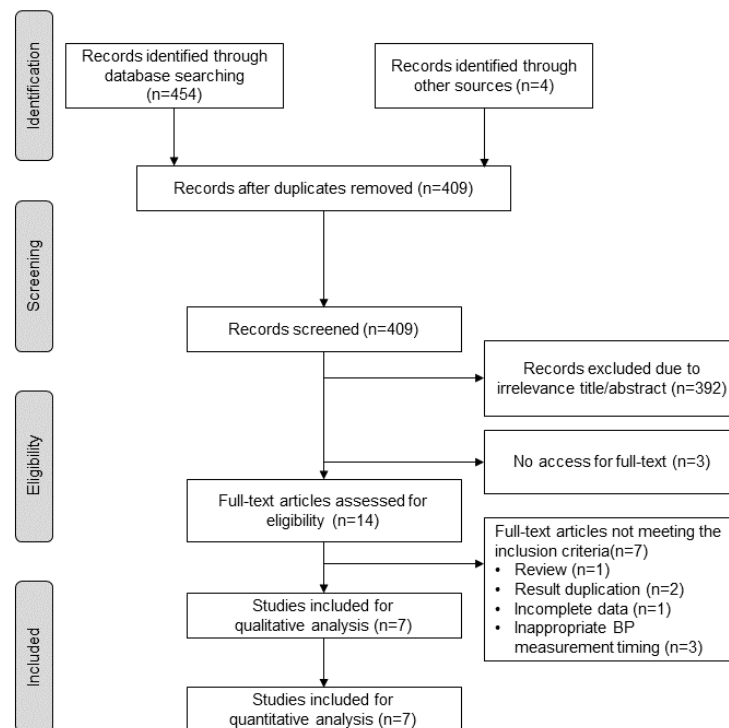


Figure 1. PRISMA flowchart for study selection

Baseline Characteristic

A total of 260 hypertensive patients from 7 distinguished studies are analyzed in this review. Six studies were considered to have good methodological quality, except a study by Alnasir (1999) was fair quality (Table 1.). Basic demographic information was quite varied among studies with the male proportion of 41% to 88% and mean age of

37.5 years to 60 years. Most studies did not specify the case definition of hypertension. Subsequently, 4 studies utilized the ambulatory method in BP measurement. The study by Eldeeb *et al.* (2020) analyzed blood pressure among individuals with and without chronic kidney disease. The summary of baseline characteristics is presented in Table 2.

Table 1. Quality Assessments Summary by Newcastle-Ottawa Scale

Author	Selection	Comparability	Exposure	Overall Quality
Salahuddin <i>et al.</i> , 2014	***	**	***	Good
Perk <i>et al.</i> , 2001	****	**	***	Good
Alinezhad-Namaghi <i>et al.</i> , 2014	***	**	***	Good
Farag <i>et al.</i> , 2020	****	**	***	Good
Eldeeb <i>et al.</i> , 2020	***	**	***	Good
Alnasir, 1999	**	**	***	Fair
Aktürk <i>et al.</i> , 2013	***	**	***	Good

Table 2. Baseline Characteristics of Included Studies

Authors	Location	Sample Size (n)	Male (%)	Age (Mean ± SD)	Case Definition	BP Measurement Method	Measurement	
							Pre-fasting (days)	Post-fasting (days)
Salahuddin <i>et al.</i> , 2014	India	15	N/A	44.6 ± 5.62	N/A	Electric Sphygmomanometer	H-1	H-1
Perk <i>et al.</i> , 2001	Israel	17	88%	56.6 ± 6.9	N/A	Ambulatory	H-7	H+7
Alinezhad-Namaghi <i>et al.</i> , 2014	Iran	6	33%	60 ± 9	Cardiologist decision (daily BP ≥140/90)	Ambulatory	H-1	H-10
Farag <i>et al.</i> , 2020	Palestine	120	50%	37.5 ± 6.6	JNC-7	Mercury Sphygmomanometer	H-7	H+7
Eldeeb <i>et al.</i> , 2020	Egypt	71	41%	57.14±14.5	N/A	Ambulatory	H-7	H+7
Alnasir, 1999	Bahrain	11	45%	56.6±11.35	N/A	Mercury Sphygmomanometer	H-7	H-7
Aktürk <i>et al.</i> , 2013	Istanbul	20	50%	52±14	N/A	Ambulatory	H-30	H-7

Blood Pressure Changes

Random-effect pooled analysis of SBP and DBP demonstrated significant reduction after Ramadan fasting (SMD=-0.77, 95%CI [-1.18—-0.36], p=0.0002 and SMD=-0.79, 95%CI [-1.35—-0.24], p=0.005; respectively). The forest plot is presented in Figure 2. These reductions could be considered as moderate effects (0.5≤SMD<0.8). Both SBP and DBP had high heterogeneity (I²= 74%, p<0.0001 and

I²= 86%, p<0.001). Subsequently, sensitivity analysis by removing Salahuddin *et al.* (2014) reduced heterogeneity in both SBP (I²=44%, p=0.10) and DBP (I²= 70% dan p=0.003) analysis without any significant change in the result (SMD=-0.64, 95%CI [-0.92—-0.35], p<0.0001 for SBP and SMD=-0.51, 95%CI [-0.89—-0.12], p=0.01 for DBP). Visual inspection of the funnel plot showed asymmetrical structure, indicating publication bias (Figure 3).

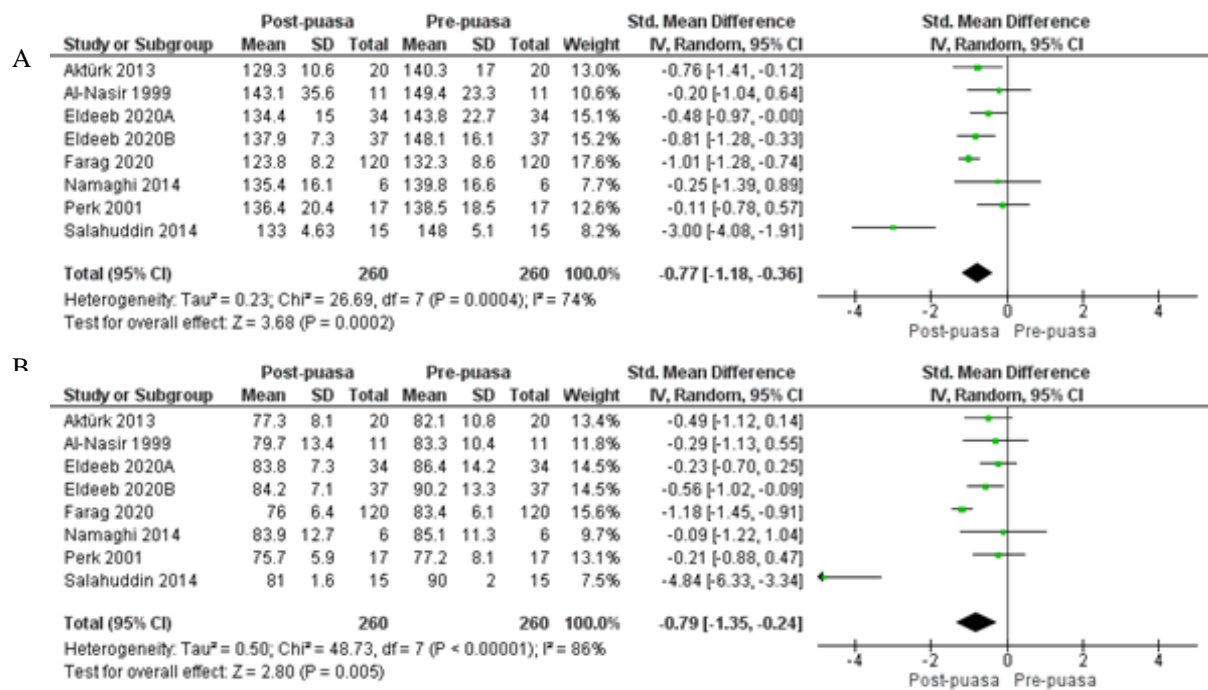


Figure 2. Ramadan Fasting Pooled Effects to (A) SBP and (B) DBP

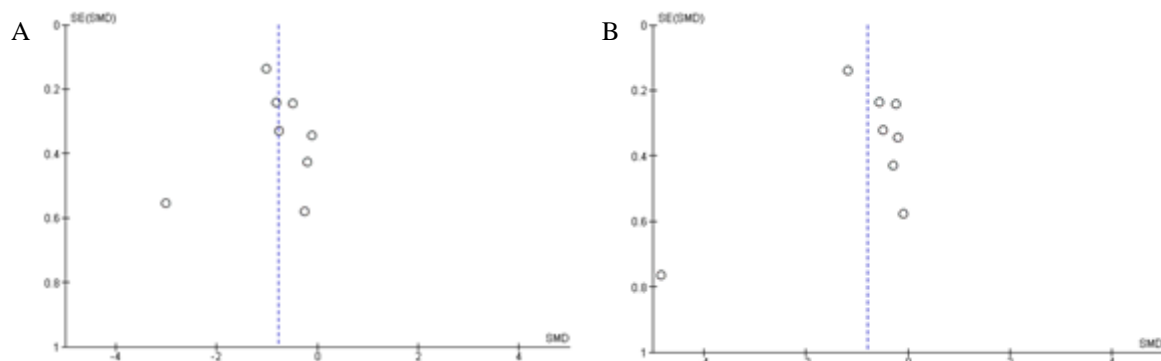


Figure 3. Funnel Plot of Pooled Analysis (A) SBP and (B) DBP

DISCUSSION

The current meta-analysis provides evidence regarding the effect of RF on BP in hypertensive patients. RF significantly reduced both SBP and DBP in moderate effects. Consistent with these findings, a recent meta-analysis demonstrated a significant reduction of SBP by RF in healthy adults.¹² However, the effect estimate was considered small (SMD=-0.51, 95%CI [-0.38—-0.11], p = 0.001). Our findings may elucidate inconclusive conclusions in previous systematic reviews regarding the effect of RF on BP in hypertensive patients.⁷

The exact mechanism of how RF influence BP in the hypertensive patient is scarce. It is suggested that during fasting, fewer free radicals are synthesized in mitochondria and lead to less cellular oxidative injury, especially to endothelial cells. Subsequently, acute hormonal adaptation, such as the Insulin-like Growth factor, is at its peak in the early days of fasting.¹³ Natriuresis is also a possible mechanism since there is a change in salt intake.¹⁴ Contrary to these, one article mentioned RF could potentially cause hypertension by activation of the renin-angiotensin system.¹⁵ Dehydration during RF potentially increases Angiotensin II levels and blood pressure.

Besides, an increase in plasma osmolality activates baroreceptors followed by arginine/vasopressin release and water retention. However, this theory is questionable since it was not supported with strong evidence and it seems implausible if 30-days of RF can lead to chronic disease such as HT. Hence, further studies are required to explain the mechanisms of RF towards BP.

Our findings could be base on lifestyle modification alternatives in hypertensive patients. Certainly, with some modification such as drinking and eating time since RF has a unique pattern. The study by Grundler *et al.*, (2020) gracefully demonstrated fasting ranging from 4 to 41 days significantly reduced BP in hypertensive patients, even when antihypertensive medications are ceased.

Current meta-analysis has several limitations. First, both analyses showed high heterogeneity which may be caused by relatively small sample and variation of the measurement method. A publication bias may also cause high heterogeneity, yet after removing the respective study, the result remained significant. Most studies did not report the case definition of HT and the specific duration of Ramadan fasting. Finally, most studies did not mention antihypertensive usage by the participant which may distort the result. Further studies are required to cover these limitations, especially with a larger sample size.

CONCLUSION

Ramadan fasting reduces both SBP and DBP in hypertensive patients. Fasting can be life modification alternatives in managing HT. However, further and larger studies are required to justify this result.

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