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Original article

Effect of fluid replacement during 60-minutes of moderate-intensity running on splanchnic blood flow

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Abstract

Background: Exercise-induced splanchnic hypoperfusion has been linked to impaired gastrointestinal function and associated symptoms. The effectiveness of fluid replacement in protecting against splanchnic hypoperfusion is less clear.
Objective: To evaluate the effects of fluid replacement during 60-minutes of moderate-intensity running on the splanchnic blood flow (SBF) using non-invasive Doppler ultrasound.
Methods: Seven healthy men aged 35.4 ± 7.0 years participated in two 60 minute running trials at moderate-intensity: the first trial with no water replacement (NW) followed by the second trial with ambient temperature water (28 - 29°C) replacement (AW). A minimum interval of 48 hours was introduced for the washout period between the trials. SBF was determined by Doppler ultrasound of the superior mesenteric artery (SMA) and portal vein (PV) before and immediately after the run. The core body temperature (Tcore) was also measured rectally.
Results: Running for 60-minutes significantly decreased the SMA flow by 31.2% (425.5 ± 98.0 mL/min to 291.7 ± 79.1 mL/min; $P = 0.002$) in NW and a non-significant decrease of 9.8% (497.2 ± 144.7 mL/min to 438.4 ± 103.1 mL/min; $P = 0.076$) in AW. The PV flow decreased by 50.6% (688.7 ± 81.9 mL/min to 333.6 ± 65.6 mL/min; $P < 0.001$) in NW and a non-significant decrease of 18.6% (718.9 ± 131.3 mL/min to 574.2 ± 145.9 mL/min; $P = 0.069$) in AW. At 60-minutes, Tcore showed a significant increase from baseline by 2.19°C ($P < 0.001$) in NW and 1.86°C ($P < 0.001$) in AW, but there was no significant difference in Tcore at 60-minutes between NW and AW.
Conclusion: Fluid replacement during 60-minutes of moderate-intensity running reduces splanchnic hypoperfusion, but not Tcore. This indicates that running-associated gut hypoperfusion may be prevented by fluid replacement during exercise.

Keywords: Doppler ultrasound, portal vein, splanchnic hypoperfusion, superior mesenteric artery.

Prolonged exercise poses a large physiological adaptation to distribute blood supply to active muscles, the cardiorespiratory system, and the skin to meet the altered demands for oxygen, nutrients, and body temperature regulation.[1] These changes are associated with decreased blood flow to the gastrointestinal (GI) tract [2] and may impair intestinal function by impairing the absorption of fluid, electrolytes, and nutrients. An impaired GI system can cause serious GI problems, such as intestinal ischemia [3], loss of the intestinal mucosal barrier with bacterial translocation [4], and systemic inflammation [5] that negatively affect 25.0% - 70.0% of endurance athletes [6, 7] in athletic performance and recovery after exercise. Although the etiology of exercise-induced GI distress is multifactorial, GI ischemia due to splanchnic hypoperfusion is often explained as the main pathophysiological mechanism for its occurrence. [7 - 9]

Exercise-induced splanchnic hypoperfusion is a compensatory response aimed at maintaining sufficient stroke volume to prevent a decline in cardiac

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output during exercise. [10] Changes in hemodynamics have been noted to depend on workload, with increases in exercise duration or intensity exacerbating these effects. [10] Consequently, this leads to a reduction in splanchnic blood flow (SBF) by 30.0% - 60.0% after 30 minutes of exercise at 60.0% - 70.0% of aerobic capacity. [4] With longer durations and higher intensities, the decrease in SBF can reach up to 80.0%. [11] These responses tend to be more pronounced in warm environments [12] and hypohydration. [13] It is important to acknowledge that previous studies primarily concentrated on cycling; therefore, the findings may not necessarily apply to runners. This distinction arises from variations in muscle usage and the occurrence of GI symptoms, which differ between running and cycling. [6] These discrepancies could also have a distinct impact on systemic blood flow.

Dehydration, fluid restriction, and water loss through sweat during prolonged exercise exacerbate splanchnic hypoperfusion [11] and increase GI dysfunction. [14, 15] Dehydration is known to increase the core body temperature (Tcore), which is already high during exercise, leading to more hyperthermia. [16] To combat this, replacing fluids during prolonged exercise, particularly in the hot environments is beneficial by reducing dehydration and lessening the rise in Tcore. [17] Despite the importance of maintaining hydration during exercise, no studies have investigated the effect of fluid replacement on SBF and Tcore during prolonged running. Therefore, the present study aimed to assess the effect of water replacement during 60 minutes of moderate-intensity running on SBF and core body temperature. The results of this study would provide valuable insights for optimizing fluid replacement strategies for individuals to protect against impairment of GI blood flow during prolonged exercise.

Materials and methods

Study design

This was an experimental design study comprising two trials: no water replacement (NW) then, ambient temperature water replacement (AW), with a minimum interval of 48 hours separation between trials as a washout period. Subjects were required to run for 60-minutes on a motorized treadmill at a speed of 70.0% of maximal oxygen uptake (VO_2max) in a controlled environment room (temperature 28 - 29 °C and 60.0% - 70.0% relative humidity, RH) at the sports and exercise medicine research laboratory the Faculty of Medicine, Chulalongkorn University, Thailand. Doppler ultrasound was used to measure SBF via the superior mesenteric artery (SMA) and portal vein before and immediately after each running experiment. All subjects were informed of the benefits and risks of the study, and each subject provided written informed consent before participation. The study protocol has been approved by the Ethics Committee of the Faculty of Medicine, Chulalongkorn University (COA no. 887/2022).

Subjects

Seven healthy men between the ages of 18 and 45 years were recruited into the study. All subjects were screened by a health history questionnaire and physical examination performed by a physician. Eligibility criteria included no significant health issues including cardiovascular disease, diabetes mellitus, chronic kidney disease, and GI problems such as inflammatory bowel diseases, celiac disease, diarrhea, GI bleeding, and colorectal cancer. All subjects were physically active at least 3 days per week and had at least 3 months of running experience. Candidates with obesity (body mass index > 30 kg/m^2), elevated blood pressure (blood pressure > 120/80 mmHg), pre-existing conditions that affected thermoregulation or physical performance, such as acute infections and injuries, and a lack of ability to complete a 60-minute moderate-intensity run (70.0% VO_2max) were excluded.

Screening and maximum oxygen consumption (VO_2max) test

Subjects completed a preliminary screening and testing session that included a brief exercise history, body composition measurement including height, weight, and % body fat (InBody770, Korea) and a VO_2max test using the modified Balke protocol [18] on a motorized treadmill (Nautilus, SportseriesT518). This was followed by a determination of the treadmill speed at 70.0% of VO_2max, where subjects ran continuously for at least 10-minutes. The average speed was obtained for running protocol to be used in the exercise trials.

Exercise trials

The subjects arrived at the laboratory in the morning, after an 8-hour fast and a 24-hour period of abstaining from exercise and alcohol. Following all baseline

measurements an experimental run with (AW) or without a fluid replacement (NW) was performed. The running protocol was set at a speed corresponding to 70.0% VO_2max. All subjects were required to run at a constant speed for 60-minutes. In AW trial, the water bottles were prepared to be served at ambient temperature in 6 equal portions, dispensed every 10 minutes, while no water was provided in the NW trial.

Fluid loss

Upon arrival at the laboratory, subjects provided an initial urine sample to determine urine specific gravity to determine hydration status. If the subject was dehydrated (urine specific gravity > 1.030), 500 ml of water would be provided, and another urine assessment was repeated 30 minutes later. The estimation of fluid loss with exercise was determined by measuring the change in body weight before and after each run. All subjects were required to void and thoroughly dry their body with a towel before measuring body weight. The amount of fluid loss will be calculated in both the NW and AW trials. The amount of fluid loss estimated from the NW trial was used as an individual fluid replacement in the AW trial.

Examination of splanchnic blood flow

All subjects underwent a 20-minute rest period prior to baseline SBF measurement. A transcutaneous ultrasound duplex system (Vivid IQ, GE Healthcare), consisting of a real-time sector scanner (3.5 MHz) with a pulsed Doppler flowmeter (3.0 MHz), was used to image the superior mesenteric artery (SMA) and portal vein (PV) and assess flow velocity and diameter of the blood vessels. B-mode was used to determine the angle between the incident ultrasound beam and the long axis of the vessel. Visualization of the SMA was performed in the sagittal plane. The sample volume is positioned in the SMA just distal to the origin from the abdominal aorta, as mentioned in previous work [19], while ensuring separation from the celiac artery through Doppler waveforms. Additionally, a longitudinal image of the portal vein was obtained using a subcostal approach. The sample volume cursor was placed at the central part of the vein, between the splenic and superior mesenteric veins' confluence and the division into the left and right hepatic branches. This method enables the accurate assessment of the hemodynamics of the portal vein. The calculation of time-averaged mean velocity (TAMV) involved determining an average value from at least two consecutive cardiac cycles. Reproducibility tests were conducted to assess the reliability of the measurements using the Intraclass Correlation Coefficient (ICC). The results indicated ICC values of 0.658 for SMA blood flow and 0.600 for PV blood flow. All tests were recorded in video files using the duplex mode for subsequent analysis.

Blood flow was calculated from TAMV and the vessel diameter (d) during systole, using the formula $TAMV \times \pi \times 4^{-1} \times d^2$. The vascular cross-sectional area was assessed during the systolic phase [20, 21], with real-time synchronization using an electrocardiogram lead. The electronic caliper was placed near the sample volume cursor, and a manual line was drawn along the length of the vessel. Measurements of the peak systolic diameter were then obtained by hand, perpendicular to the vessel wall. This process was repeated three times to obtain an average measurement value.

Doppler ultrasound was performed before running and immediately (no longer than 5 minutes) after running trial. All Doppler ultrasound measurements and their evaluation were performed by the same radiologist while subjects were in a supine position and instructed to momentarily hold their breath to minimize the interference of respiratory movements.

Examination of core body temperature

The measurement of Tcore was performed to observe the impact of exercise and fluid replacement on body heat accumulation. A rectal thermocouple (YSI 400 series, interchangeability tolerance of ± 0.1 °C) was inserted to a depth of 10 cm beyond the external anal sphincter. Tcore was continuously monitored, and the temperature value was recorded every 5 minutes throughout the 60-minute running period.

Statistical analysis

Statistical analyses were performed using STATA (Stata/SE 17.0). Data are presented as mean ± standard deviation (SD) and 95% confidence interval (CI) for normally distributed data. To evaluate repeated measures and changes in the outcome variable at multiple time points of Tcore a generalized estimating equation (GEE) and linear mixed-effects model were employed to account for fixed and random effects. A paired samples *t* - test was used to compare the mean changes in SMA and PV blood flow between trials and at 60-minutes to the baseline value. $P < 0.05$ was considered statistically significant.

Results

Subjects

Baseline data from seven endurance runners are shown in **Table 1.** The median time between trials was 9 days.

Laboratory condition

The room temperature in the laboratory was controlled and no difference between 2 trials (NW: 28.4 ± 0.2°C, RH 63.1 ± 2.2%; AW: 28.4 ± 0.2 °C, RH: 63.4 ± 1.8, $P = 0.726$) was observed.

Body fluid loss, core body temperature, and urine specific gravity

Body fluid loss differed significantly between the two trials (NW, 1.4 ± 0.2 kg vs. AW, 0.3 ± 0.3 kg, $P < 0.001$). Tcore progressively increased during exercise, reaching 38.6 ± 0.4 °C in NW and 38.5 ± 0.4 °C in AW at 60 minutes, with no significant difference observed between the trials ($P = 0.453$). **(Figure 1)** No significant difference was observed in the average rate of increase in Tcore between the NW and AW trials ($P = 0.963$). Nevertheless, notable distinctions were found in the rate of increase of Tcore, specifically during the last fifteen minutes of the run, with a greater increase observed in the NW trial compared to the AW trial. **(Table 2)** Baseline urine specific gravity was 1.012 ± 0.008 for NW and 1.012 ± 0.007 for AW, with no significant difference between trials ($P = 0.920$). All urine samples contained a value of no more than 1.030, indicating that none of the subjects was dehydrated.

Splanchnic blood flow

Superior mesenteric artery (SMA)

Comparisons of SMA blood flow between NW and AW are presented in **Table 3**. The SMA flow significantly decreased in NW (133.8 ± 69.9 mL/min, $P = 0.002$), but not significantly decreased in AW trial (58.8 ± 72.5 mL/min, $P = 0.076$). The baseline measurements of the SMA blood flow do not exhibit a significant difference between the trials.

Portal vein (PV)

Comparisons of PV blood flow between NW and AW are presented in **Table 3**. The PV blood flow significantly decreased in the NW trial (355.1 ± 114.8 mL/min, $P < 0.001$), but not significantly reduced in the AW trial (144.7 ± 173.6 mL/min, $P = 0.069$). The baseline measurements of the PV blood flow did not exhibit significant differences between the trials.

Table 1. Baseline characteristics of the subjects (n = 7).

Characteristics	Mean ± SD
Age (years)	35.4 ± 7.5
Height (cm)	171 ± 2.9
Body weight (kg)	66.9 ± 8.7
Body mass index (BMI) (kg/m^2)	22.8 ± 2.5
Body fat (%)	14.8 ± 5.9
Resting heart rate (bpm)	59.8 ± 9.6
Resting blood pressure	
Systolic blood pressure (mmHg)	111.7 ± 9.9
Diastolic blood pressure (mmHg)	75.1 ± 4.7
VO_{2max} (mL/kg/min)	53.0 ± 5.1
70.0%VO_{2max} Speed (km/h)	10.2 ± 1.1
Baseline Tcore (°C)	36.5 ± 0.2

VO_2max, maximum oxygen consumption; Tcore, core body temperature; bpm, beats per minute. All data were collected during the preliminary visit to gather baseline characteristics, except for baseline Tcore, which represents the average core temperature before both trials.

Table 2. Comparison of Tcore change between AW and NW (n = 7).

Outcome/time (min)	AW Change from baseline (95%CI)	NW Change from baseline (95%CI)	Difference between trial (95%CI)	*P* - value
5 min	0.3 (0.1, 0.4)	0.2 (0.1, 0.4)	0.03 (-0.2, 0.2)	0.788
10 min	0.5 (0.4, 0.7)	0.6 (0.4, 0.8)	-0.04 (-0.3, 0.2)	0.687
15 min	0.9 (0.7, 1.1)	0.9 (0.7, 1.1)	-0.01 (-0.2, 0.2)	0.893
20 min	1.2 (1.0, 1.4)	1.2 (1.1, 1.4)	-0.07 (-0.3, 0.1)	0.502
25 min	1.3 (1.1, 1.5)	1.4 (1.2, 1.7)	-0.1 (-0.3, 0.1)	0.227
30 min	1.5 (1.3, 1.7)	1.6 (1.4, 1.8)	-0.1 (-0.3, 0.1)	0.283
35 min	1.6 (1.3, 1.9)	1.7 (1.5, 2.0)	-0.1 (-0.4, 0.1)	0.18
40 min	1.7 (1.4, 2.0)	1.9 (1.6, 2.2)	-0.2 (-0.4, 0.1)	0.14
45 min	1.8 (1.5, 2.1)	2.0 (1.7, 2.3)	-0.2 (-0.4, -0.0)	0.032
50 min	1.9 (1.5, 2.2)	2.0 (1.7, 2.4)	-0.2 (-0.4, 0.0)	0.107
55 min	1.8 (1.4, 2.2)	2.1 (1.7, 2.5)	-0.3 (-0.5, -0.1)	0.005
60 min	1.9 (1.5, 2.3)	2.2 (1.8, 2.6)	-0.3 (-0.5, -0.1)	0.002
Change of Tcore (°C/min)	0.031 (0.026, 0.037)	0.036 (0.030, 0.041)	-0.003 (-0.123, 0.117)	0.963

Tcore, core body temperature; NW, no water replacement; AW, ambient-temperature water replacement. The analyses were performed using the linear mixed-effects model adjusted for the change from baseline value.

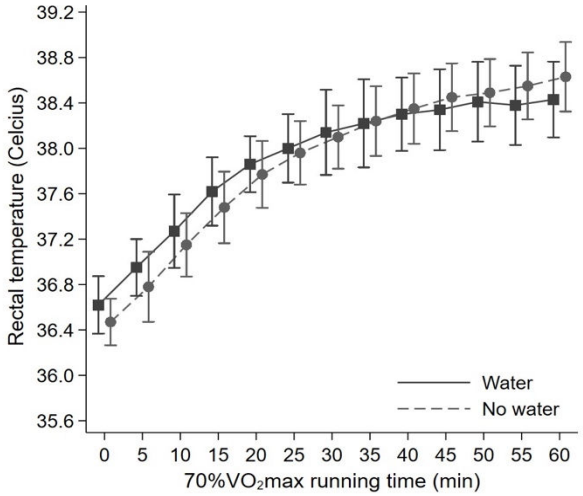

Figure 1. Rectal temperature at baseline and every 5 min until 60 min during 70.0% VO_2max running in no water and water replacement trials. Values are mean (95%CI). The solid line indicates water replacement; Dashed line indicates no water replacement. At 60 minutes, there were no significant difference in rectal temperatures between the trials ($P = 0.453$).

Table 3. The comparison of splanchnic blood flow between AW and NW (n = 7)

Outcome/Time(min)	AW Mean ± SD	NW Mean ± SD	Mean difference (95%CI)	*P* - value
SMA flow (mL/min)				
0 - min	497.2 ± 144.7	425.5 ± 98.0	71.7 (-37.8, 181.3)	0.160
60 - min	438.4 ± 103.1	291.7 ± 79.1	146.8 (45.6, 247.9)	0.012
△ from baseline (%)	-9.8 ± 16.6	-31.2 ± 13.0	-21.4 (-36.0, -6.8)	0.011
PV flow (mL/min)				
0 - min	718.9 ± 131.3	688.7 ± 81.9	30.2 (-79.9, 140.3)	0.527
60 - min	574.1 ± 145.9	333.6 ± 61.6	240.5 (95.9, 385.1)	0.007
△ from baseline (%)	-18.6 ± 24.0	-50.6 ± 12.5	-32.1 (-57.8, -6.3)	0.023

AW, ambient temperature water replacement; NW, No water replacement; △, change.
[a]*P* - value corresponds to paired samples *t* - test.

Discussion

The present study aimed to investigate the acute effect of water intake during a 60-minute run at 70.0% VO_2max on splanchnic blood flow in healthy men. The primary finding demonstrated that running exercise reduces splanchnic blood flow. Rehydration with ambient temperature water during running significantly reduces splanchnic hypoperfusion in both the SMA and PV. Moreover, replacement with ambient temperature water reduces fluid loss due to exercise. Additionally, fluid replacement did not affect Tcore at the end of 60-minute run. Our study highlights the importance of water replacement to mitigate gut hypoperfusion during moderate-intensity endurance run.

In previous studies [11, 22], it was observed that a lack of fluid replacement during 60 minutes of cycling at 70.0% VO_2max resulted in an 80.0% reduction in PV flow, while water replacement resulted in approximately a 50.0% reduction, as measured by Doppler ultrasound. The larger reduction in PV flow compared to our study raises several considerations. Firstly, the inclusion of a caloric breakfast before exercise in those studies may have influenced the observed results, as the ingestion of food and fluids can impact splanchnic and systemic hemodynamics. [23] In contrast, no food or caloric beverages were provided before the trials in our study. Secondly, the report on "zero flow" velocity in two subjects could potentially raise questions about the technique used in those studies that might have influenced the overall findings. It is noteworthy that in our study, there were no statistically significant differences in the baseline values of blood flow of SMA and PV between the trials. This finding reflects non-significant day to day variation and the reproducibility of our measurement of SBF using ultrasound techniques. Lastly, it appears that runners experience a higher incidence of gastrointestinal issues than other athletes, such as cyclists. [6] Although we hypothesized that these factors may have differentially influenced the results of the investigations, without fluid replacement, the magnitude of reduction in SBF during running unexpectedly resembled what was observed in cycling with comparable exercise duration and intensity. [24]

The previous study indicated that fluid restriction during a 60-minute running session can worsen GI dysfunction by reducing GI blood flow and causing hyperthermia. [25] The reduction in blood flow to the GI tract during exercise may contribute to higher temperatures in the abdominal cavity, due to decreased heat dissipation. [10] Consistent with the study by Lambert GP, *et al.* [14], Tcore measured in this study did not show a significant difference between the NW and AW at 60 minutes. Nevertheless, we observed a distinct divergence in the incremental rate of Tcore between NW and AW after 45 minutes of running. It is very likely that NW may generate a higher Tcore progression rate compared to AW with a longer running duration. Thus, ingestion of water at ambient temperature can prevent rising of Tcore for at the last 15 minutes and potentially reduces risk of hyperthermia associated with prolonged running exercise.

The study's findings revealed a significant improvement in splanchnic hypoperfusion as a result of running exercise among healthy men through the administration of water in the AW trial. It should be noted that there is no specific regimen for the prevention or treatment of exercise-induced splanchnic hypoperfusion. However, our findings highlight the important role of proper fluid intake spreading throughout the duration of exercise. Such an approach serves a dual purpose: firstly, mitigating the risk of GI dysfunction and GI symptoms associated with runner's GI ischemia; and secondly, maintaining an optimal body temperature. These insights can be particularly valuable as advisory recommendations in the clinical setting for endurance runners.

The present study has several limitations that should be considered. Firstly, it was not specifically designed to investigate the effects of blood flow on GI dysfunction. Therefore, there are no data to support the effect of fluid replacement in preventing the reduction in blood flow and reducing the GI injury reported in endurance athletes. Secondly, the study only included healthy men; therefore, the findings may not apply to cyclists or athletes engaging in other types of endurance exercise. Additionally, Doppler ultrasound was only performed before and after the running trials, and changes in splanchnic perfusion during running are unknown. It is important to note that the Doppler ultrasound assessment in this study yielded a low ICC value, potentially attributable to factors like ultrasound image quality and the presence of bowel gas, which could impact the reliability of the measurements. Moreover, we did not obtain the blood

pressure information while the SBF measurement was performed. Rather, we used a 5-minute window period after running for ultrasound scanning. Consequently, hemodynamic decay after exercise could not be assessed, and it may affect the extrapolation of splanchnic blood flow during exercise. Finally, the study only investigated the effect of water at ambient temperature (28°C), so the findings may not be applicable to other temperatures or other types of sports drinks, such as those containing carbohydrates, proteins, and electrolytes. These limitations suggest the need for further research to investigate the effects of various types of fluid and other factors on splanchnic blood flow and GI dysfunction in different types of endurance athletes.

Conclusion

The findings of this study suggest that fluid replacement during 60-minute moderate-intensity running can attenuate the splanchnic hypoperfusion. This study underscores the importance of fluid replacement during running to maintain blood flow of the splanchnic organs. Additionally, the replacement of ambient temperature fluid reduces the rising rate of Tcore after 45-minutes of running at moderate intensity in a slightly warm condition.

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Conflict of interest

All authors have completed and submitted the International Committee of Medical Journal Editors Uniform Disclosure Form for Potential Conflicts of Interest. None of the authors disclose any conflict of interest.

Data sharing statement

The present review is based on the references cited. All data generated or analyzed during the present study are included in this published article and the citations herein. Further details, opinions, and interpretation are available from the corresponding author on reasonable request.

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