Original Article

Active Ankle Movements Improve Renal Blood Flow in Community-Dwelling Elderly

Tudpor K, PhD[1], Sripongngam T, PhD[2], Kanpittaya J, MD[3], Takong W, MD[3]

[1] Faculty of Public Health, Mahasarakham University, Mahasarakham, Thailand
[2] Department of Health and Sport Science, Faculty of Education, Mahasarakham University, Mahasarakham, Thailand
[3] Department of Radiology, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand

Background: Renal blood flow is important for maintaining kidney functions and is controlled by an autonomic nervous system (ANS). An ankle exercise is widely used for improving blood flow in lower limb, but its effects on renal blood flow have not been examined.

Objective: To investigate the effects of the active ankle movements (AAM) on renal arterial hemodynamics and autonomic nervous system (ANS) responses in community-dwelling elderly participants.

Design: The present study is a prospective randomized controlled trial. Twenty-six community-dwelling elderly participants were randomized to control (n = 13) and AAM (n = 13) groups.

Materials and Methods: The AAM group was instructed by physiotherapists to perform the combined active movements of plantar flexion, dorsi flexion, inversion, and eversion at the frequency of 60 times/min for 15 min; while the control group was instructed to rest for another 15 minute. Primary outcomes [volumetric arterial blood flow (VF), peak systolic velocity (PSV), end diastolic velocity (EDV), and resistive index (RI)] were determined by radiologists using a Doppler ultrasound on the left renal artery at baseline and post-intervention. Secondary outcomes [heart rate variability (HRV) parameters low-frequency spectral power (LF), high-frequency spectral power (HF), LF/HF ratio, standard deviation of normal-to-normal intervals (SDNN), and root mean square of successive differences (RMSSD)] were determined as ANS proxies.

Results: After the AAM, VF in the left renal artery significantly increased from 327.7±47.4 to 402.7±56.5 ml/min ($p<0.05$) whereas PSV, EDV, and RI were not changed. HRV measurements showed that LF (a proxy of sympathetic cardiac control) decreased from 5.21±0.22 to 4.85±0.15 ms^2 ($p<0.05$).

Conclusion: The AAM increased renal arterial blood flow putatively by reducing sympathetic input to the renal artery.

Keywords: Active ankle movements, Renal blood flow, Doppler ultrasound, Elderly, sympatho-vagal balance

J Med Assoc Thai 2019;102(Suppl.7): 51-5
Website: http://www.jmatonline.com

A primary function of the kidneys is to eliminate waste products from blood circulation. Kidney functions are highly dependent upon ample blood and nerve supplies. Despite relatively small sizes of the kidneys, renal blood flow (RBF) is approximately 25% of the total cardiac output(1). The kidneys are highly sensitive to changes in RBF, which can be measured with a Doppler ultrasound in form of volumetric arterial blood flow (VF) together with other parameters including peak systolic velocity (PSV), end diastolic velocity (EDV), and resistive index (RI)(2). RBF is regulated by autonomic innervation. An input from the sympathetic nerve can cause vasoconstriction and a reduction in RBF(3). In contrast, the parasympathetic (vagus) nerve is also present in the kidneys and associated with RBF(4).

In principle, the sympatho-vagal balance is important for cardiovascular system homeostasis and can be measured as heart rate variability (HRV). The HRV measurements consist of time and frequency domains. The time domain analysis includes standard deviation of all normal R-R intervals (SDNN), square root of the mean of the squared successive differences in R-R intervals (RMSSD) and percentage of R-R intervals that are at least 50 ms different from the previous interval (pNN50)(5). The frequency domain is composed of low frequency (LF, 0.04 to 0.15 Hz), high frequency (HF, 0.15 to 0.40 Hz), and low to high frequency ratio (LF/HF)(6). The SDNN is a representative of overall HRV (autonomic activity). LF predominantly represents a sympathetic outflow whereas HF, RMSSD and pNN50 designate vagal activity. LF/HF ratio reflects sympatho-vagal balance(7). Even though the HRV is related to renal functions, its association with RBF is still elusive.

Correspondence to:
Tudpor K.
Faculty of Public Health, Mahasarakham University, Khamrieng, Kantarawichai, Mahasarakham 44150, Thailand.
Phone: +66-95-8983096, **Fax:** +66-43-754353
E-mail: kukiat.t@msu.ac.th

How to cite this article: Tudpor K, Sripongngam T, Kanpittaya J, Takong W. Active Ankle Movements Improve Renal Blood Flow in Community-Dwelling Elderly. J Med Assoc Thai 2019;102(Suppl.7): 51-5.

Any conditions that restrict renal arterial blood flow such as renal artery stenosis, atherosclerosis, and advancing age can reduce the sizes and functions of the kidneys[8]. The age-related arterial stiffening can be preserved by a pharmacological therapy, nutritional therapy, and exercise therapy[9]. It has been reported that physical movements affected RBF, for example, a single bout of strenuous exercises reduced RBF by 51% due to sympathetic outflow-induced vasoconstriction of renal artery[10]. However, light exercises (indicated by a stable level of sympathetic postganglionic nerve-derived norepinephrine in plasma) such as the AAM are recommended for the elderly[11,12]. Until now; however, the effects of the light exercises on RBF have not been elucidated. This present study was aimed to investigate effects of the AAM on renal hemodynamics and HRV in the community-dwelling elderly.

Materials and Methods

Study design

A prospective randomized controlled trial has been registered to the Thai Clinical Trials Registry (TCTR 20181024001) and approved by the Ethical Review Committee for Human Research, Mahasarakham University (014/2559). The study was conducted at Srinagarind Hospital, a tertiary care university medical center. Written informed consent forms were obtained from all patients.

Participants and baseline assessments

Thirty-four community-dwelling elderly participants were assessed for eligibility. Eight participants were dropped out from the program due to initial findings of hydronephrosis and nephrolithiasis. Twenty-six participants were randomly allocated to control group (n = 13) and AAM group (n = 13) (Figure 1). Inclusion criteria were age 60 years old or more, no kidney diseases, ability to communicate, and informed consent. Exclusion criteria were heart diseases, cognitive impairments, taking any medication, and ankle joint pain. After recruitment, the participants were evaluated for urine protein concentration, blood pressure, body mass index (BMI) and other demographic data. The data of the completed participants are shown in Table 1. The participants were re-confirmed for the absence of nephrolithiasis and hydronephrosis with a Doppler ultrasound. Before the interventions, the participants were instructed to obtain enough sleep, refrain from drinking alcohol for 12 hour, and not to consume any food within 90 minute.

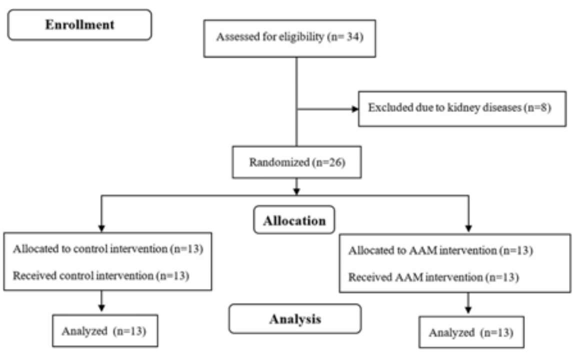

Figure 1. Design and flow of participants through the randomized controlled trial.

Intervention

Before the intervention, the participants were asked to rest in bed in supine lying position for 15 minute to acclimatize themselves. Subsequently, the ultra-short term HRV parameters were measured for 2.5 minute followed by the renal hemodynamics measurements. The participants in the AAM group performed the combined active movements of plantar flexion, dorsi flexion, inversion, and eversion at the frequency of 60 times/minute for 15 minute, which have been reported as the most effective procedures for improving the femoral blood flow[13,14]. The control participants were instructed to rest for another 15 minute. The renal hemodynamics and HRV parameters were reassessed immediately after the intervention.

Outcomes

The primary outcomes were renal hemodynamics parameters. Doppler spectral analysis was applied to measure the renal hemodynamics parameters (VF, PSV, EDV, and RI) (Profound F75 continuous-wave ultrasound, Hitachi-Aloka). The participants were requested to lie in bed in prone position to expose posterior kidneys. The ultrasound with linear 4.4 to 13 MHz probe was placed between 12th thoracic vertebra and 2nd lumbar vertebra at the position of the left kidney (5 cm lateral to the spine). Each participant was examined twice and mean of the parameters were recorded. All the procedures were conducted by experienced radiologists. The HRV parameters (LF, HF, LF/HF ratio, SDNN, RMSSD, and pulse rate), as secondary outcomes, were measured with uBioMacpa software version 1.0 (BioSense Creative Co. Ltd, Korea) on the participant's left index finger tips. Data were automatically saved into a personal computer for later analysis. Temperature and humidity in the experimental room were set to 25°C and 60 to 70%, respectively. All the

Table 1. Basic characteristics of participants at baseline

Variable	Control	Active ankle movements
Age (years)	65.0±1.1	66.5±1.7
Gender		
Male	3	2
Female	10	11
Height (cm)	153.7±2.5	153.7±1.6
Weight (Kg)	56.9±3.0	59.0±2.7
BMI (kg/m^2)	24.3±1.4	25.0±1.3
Systolic blood pressure (mmHg)	140.7±4.2	137.8±6.0
Diastolic blood pressure (mmHg)	76.1±3.2	77.1±3.8
Urine protein (mg/24 h)	47.9±18.0	27.9±7.1

experiments were performed during the same period of the day (between 1.00 to 4.00 PM) to avoid the effects of circadian rhythm on HRV[15].

Sample size calculation

Having been allocated effect size of 1.2[16], α-error level (two-sided) = 0.05, 1-β error level = 0.8, sample size per group was calculated by G*power program, providing n =12/group.

Statistical analysis

If not specified otherwise, the data are expressed as mean ± SEM. Normality of sample data was tested by Kolmogorov-Smirnov test. Means of two dependent and independent groups were compared by paired t-test and unpaired t-test, respectively. The level of statistical significance was $p<0.05$. All data were analyzed by GraphPad Prism (version 4.0 c for Mac OS X; GraphPad Software, USA).

Results

Baseline characteristics

Twenty-six participants completed the program (control, n = 13 and AAM, n = 13). All participants had normal BMI, high systolic blood pressure, and no kidney diseases (urine protein concentration <80 mg/24 h). All basic demographic data are shown in Table 1.

Active ankle movements increased renal arterial blood flow

At baselines, VF values were not significantly different between control and AAM groups (527.0±110.2 and 327.7±47.4 mL/min, respectively, $p = 0.06$) (Table 2). At the point of post-intervention, VF was not significantly changed in control group. In contrast, VF of the AAM group significantly increased from 327.7±47.4 to 402.7±56.5 mL/min ($p<0.05$). However, there are no significant changes of PSV, EDV, and RI in both control and AAM groups at the respective post-intervention points.

Active ankle movements decreased low-frequency signal of HRV and pulse rate

At baselines, LF values were not different between control and AAM groups (5.51±0.21 and 5.21±0.22 ms^2, respectively, $p = 0.18$) (Table 2). At the point of post-intervention, LF was not changed in control group. In contrast, LF of AAM group significantly decreased from 5.21±0.22 to 4.85±0.15 ms^2 ($p<0.05$). Moreover, pulse rate in both groups reduced from 67.7±2.9 to 65.2±2.6 beat/min in control group and 65.4±1.3 to 63.8±1.3 beat/min in AAM group. There are no significant changes of HF, LF/HF ratio, SSDN, and RMSSD in both control and AAM groups at the respective post-intervention points.

Discussion

The present study shows that the AAM improve renal arterial blood flow probably by reducing renal sympathetic inputs. Our conclusion is based on the following findings: 1) the AAM increases VF and 2) the AAM reduces the sympathetic tone as indicated by a decrease of LF value. As the community-dwelling elderly population are relatively less active and more vulnerable to physical injuries than younger adults, light exercises are used to maintain their health and quality of life[17]. So far, various forms of the light exercises such as walking and chair-based exercises have been shown to improve joint mobility, body balance, and cardiovascular fitness in elderly[17,18]. The AAM has been widely used as prophylactic regimen against the risk of venous thrombosis

Tables 2. Renal artery and heart rate variability parameter measurements

Group/point of measurement	Control		Active ankle movements	
	Baseline	Post-intervention	Baseline	Post-intervention
Renal artery parameter				
VF (mL/min)	527.0±110.2	479.4±100.7	327.7±47.4	402.7±56.5*
PSV (cm/s)	55.1±4.8	50.3±4.2	43.4±2.5	44.7±1.9
EDV (cm/s)	15.4±1.8	16.2±1.7	12.8±1.1	13.8±1.2
RI	0.72±0.02	0.68±0.02	0.71±0.02	0.69±0.02
Heart rate variability parameter				
lnLF (ms^2)	5.51±0.21	5.62±0.16	5.21±0.22	4.85±0.15*#
lnHF (ms^2)	5.09±0.21	5.21±4.2	5.03±0.27	4.86±0.19
LF/HF ratio	1.08±0.03	1.08±0.02	1.18±0.13	1.16±0.14
SSDN (ms)	33.6±3.9	36.9±3.7	31.0±2.6	29.3±2.6
RMSSD (ms)	29.3±4.0	32.2±3.7	27.6±3.3	25.8±2.3
Pulse rate (beat/min)	67.7±2.9	65.2±2.6*	65.4±1.3	63.8±1.3*

VF = volumetric arterial blood flow; PSV = peak systolic velocity; EDV = end diastolic velocity; RI = resistive index; lnLF = natural logarithm of low-frequency spectral power; lnHF = natural logarithm of high-frequency spectral power; SDNN = standard deviation of normal-to-normal intervals; RMSSD = root mean square of successive differences.
Data are presented as mean ? SEM. * $p<0.05$ versus respective baseline. # $p<0.05$ versus respective control

as it was able to enhance blood flow in femoral veins up to 200%[19,20]. Moreover, Nagaya et al recently evaluated the effect ankle passive movements in the community-dwelling elderly people with a near infrared spectroscopy technique and found that cerebral blood flow was significantly elevated as indicated by an increase in oxyhemoglobin level in the cerebral vessels[21]. The present study was first to demonstrate a stimulatory effect of the AAM on VF, but not on PSV, EDV, and RI.

The PSV and EDV are inversely proportional to the cross-sectional area of the vessels. A reduction in PSV and EDV are associated with an increase in the transmural pressure across the vessels in hypertensive patients[22]. In the present study, the overall PSV values in the renal artery of both groups ranged between 32 to 95 cm/s, which were in the normal range (<120 cm/s)[23]. Consequently, the RI values derived from the PSV and EDV (PSV-EDV/PSV) at baselines and post-intervention points in both groups were also in the normal range (<0.7)[24]. These findings point out that the AAM are safe to enhance the RBF without affecting the transmural pressure.

The RBF is regulated by the ANS particularly sympathetic input as depicted the LF power[25]. In the present study, apart from a decrease in the pulse rate, only the LF component of the frequency domain decreased whereas the HF and LF/HF ratio (a representative of sympatho-vagal balance) were not significantly changed after the AAM[26]. Of note, our results showed that baseline LF/HF ratios in both control and AAM groups were approximately 1 and not significantly changed after the interventions. In cardiac patients, values of LF/HF ratio higher than 4.8 correspond to sympathetic predominance and those lower than 1.3 linked to vagal modulation activity[5]. Therefore, our elderly participants in the present study were basically vagal predominant. Even though the SDNN is a primary parameter among other HRV power spectra, it has been reported that LF is more sensitive to aging than SDNN[27]. Most of the elderly participants in the present study were female. In general, the LF power spectrum in male is higher than in female[28]. However, Voss and co-workers showed that this difference disappeared upon the age of 55 years old[29]. Therefore, an unequal number of male and female with the group would not affect the values.

Conclusion

The present study demonstrates that the AAM are beneficial for enhancing renal arterial blood flow in the community-dwelling elderly individuals putatively by reducing renal sympathetic tone. This might be applied to the healthy elderly for preventing an age-related decline in renal functions.

What is already known on this topic?

Active ankle movements are beneficial for preventing deep vein thrombosis by increasing femoral blood flow. In addition, cerebral blood flow can also be improved.

What this study adds?

The community-dwelling elderly participants performing the active ankle movements showed a significant improved renal blood flow as well as reduced the fight-or-flight responses. In long term, this light procedure of exercises might be implemented to prevent the loss of renal functions in elderly.

Acknowledgements

This work was financially supported by the Health Systems Research Institute, Thailand (Project No. 60-059).

Potential conflicts of interest

The authors declare no conflict of interest.

References

1. Basile DP, Anderson MD, Sutton TA. Pathophysiology of acute kidney injury. Compr Physiol 2012;2:1303-53.
2. Viazzi F, Leoncini G, Derchi LE, Pontremoli R. Ultrasound Doppler renal resistive index: a useful tool for the management of the hypertensive patient. J Hypertens 2014;32:149-53.
3. Kannan A, Medina RI, Nagajothi N, Balamuthusamy S. Renal sympathetic nervous system and the effects of denervation on renal arteries. World J Cardiol 2014;6:814-23.
4. Layton AT. Recent advances in renal hemodynamics: insights from bench experiments and computer simulations. Am J Physiol Renal Physiol 2015;308:F951-5.
5. Milicevic G. Low to high frequency ratio of heart rate variability spectra fails to describe sympatho-vagal balance in cardiac patients. Coll Antropol 2005;29:295-300.
6. Lombardi F, Malliani A, Pagani M, Cerutti S. Heart rate variability and its sympatho-vagal modulation. Cardiovasc Res 1996;32:208-16.
7. Shaffer F, Ginsberg JP. An overview of heart rate variability metrics and norms. Front Public Health 2017;5:258.
8. Weinstein JR, Anderson S. The aging kidney: physiological changes. Adv Chronic Kidney Dis 2010;17:302-7.
9. Wu CF, Liu PY, Wu TJ, Hung Y, Yang SP, Lin GM. Therapeutic modification of arterial stiffness: An update and comprehensive review. World J Cardiol 2015;7:742-53.
10. Kawakami S, Yasuno T, Matsuda T, Fujimi K, Ito A, Yoshimura S, et al. Association between exercise intensity and renal blood flow evaluated using ultrasound echo. Clin Exp Nephrol 2018;22:1061-8.
11. Tse AC, Wong TW, Lee PH. Effect of low-intensity exercise on physical and cognitive health in older adults: a systematic review. Sports Med Open 2015;1:37.
12. Svarstad E, Myking O, Ofstad J, Iversen BM. Effect of light exercise on renal hemodynamics in patients with

hypertension and chronic renal disease. Scand J Urol Nephrol 2002;36:464-72.
13. Sochart DH, Hardinge K. The relationship of foot and ankle movements to venous return in the lower limb. J Bone Joint Surg Br 1999;81:700-4.
14. Nakayama T, Tsukada S, Hiyama T, Yamada T, Hirasawa N. Impact of active ankle movement frequency on velocity of lower limb venous flow following total hip arthroplasty. Adv Orthop 2016;2016:7683272.
15. Vandewalle G, Middleton B, Rajaratnam SM, Stone BM, Thorleifsdottir B, Arendt J, et al. Robust circadian rhythm in heart rate and its variability: influence of exogenous melatonin and photoperiod. J Sleep Res 2007;16:148-55.
16. Kato TS, Ono S, Kajimoto K, Kuwaki K, Yamamoto T, Amano A. Early introduction of tolvaptan after cardiac surgery: a renal sparing strategy in the light of the renal resistive index measured by ultrasound. J Cardiothorac Surg 2015;10:143.
17. Munro JF, Nicholl JP, Brazier JE, Davey R, Cochrane T. Cost effectiveness of a community based exercise programme in over 65 year olds: cluster randomised trial. J Epidemiol Community Health 2004;58:1004-10.
18. Anthony K, Robinson K, Logan P, Gordon AL, Harwood RH, Masud T. Chair-based exercises for frail older people: a systematic review. Biomed Res Int 2013;2013:309506.
19. Kwon OY, Jung DY, Kim Y, Cho SH, Yi CH. Effects of ankle exercise combined with deep breathing on blood flow velocity in the femoral vein. Aust J Physiother 2003;49:253-8.
20. McNally MA, Cooke EA, Mollan RA. The effect of active movement of the foot on venous blood flow after total hip replacement. J Bone Joint Surg Am 1997;79:1198-201.
21. Nagaya S, Hayashi H, Fujimoto E, Maruoka N, Kobayashi H. Passive ankle movement increases cerebral blood oxygenation in the elderly: an experimental study. BMC Nurs 2015;14:14.
22. Bellinazzi VR, Cipolli JA, Pimenta MV, Guimaraes PV, Pio-Magalhaes JA, Coelho-Filho OR, et al. Carotid flow velocity/diameter ratio is a predictor of cardiovascular events in hypertensive patients. J Hypertens 2015;33:2054-60.
23. Granata A, Fiorini F, Andrulli S, Logias F, Gallieni M, Romano G, et al. Doppler ultrasound and renal artery stenosis: An overview. J Ultrasound 2009;12:133-43.
24. Platt JF, Rubin JM, Ellis JH. Distinction between obstructive and nonobstructive pyelocaliectasis with duplex Doppler sonography. AJR Am J Roentgenol 1989;153:997-1000.
25. Umetani K, Singer DH, McCraty R, Atkinson M. Twenty-four hour time domain heart rate variability and heart rate: relations to age and gender over nine decades. J Am Coll Cardiol 1998;31:593-601.
26. Malliani A, Pagani M, Lombardi F, Cerutti S. Cardiovascular neural regulation explored in the frequency domain. Circulation 1991;84:482-92.
27. Bigger JT Jr, Fleiss JL, Steinman RC, Rolnitzky LM, Schneider WJ, Stein PK. RR variability in healthy, middle-aged persons compared with patients with chronic coronary heart disease or recent acute myocardial infarction. Circulation 1995;91:1936-43.
28. Jensen-Urstad K, Storck N, Bouvier F, Ericson M, Lindblad LE, Jensen-Urstad M. Heart rate variability in healthy subjects is related to age and gender. Acta Physiol Scand 1997;160:235-41.
29. Voss A, Schroeder R, Heitmann A, Peters A, Perz S. Short-term heart rate variability—influence of gender and age in healthy subjects. PLoS One 2015;10:e0118308.