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Original Article

TCM "Bigu" effect on serum vasoactive substances and possible primary prevention of cardiovascular diseases in sub-healthy Chinese women

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Abstract: Objective: To observe the intervention effect of TCM Bigu on serum vasoactive substances, as well as major physiological and biochemical indicators, and cardiovascular disease prevention in sub-healthy Chinese women who felt unwell but had no clear disease index. Methods: Eleven sub-healthy Chinese women aged 25-62 years, joined in and completed a 7-day TCM Bigu intervention. Changes in serum vasoactive substances (eNOS, NE, ET-I, ANG-II, INS), body composition, and major biochemical indicators as well as daily calorie intake at the beginning and end of the intervention were detected. Results: The serum eNOS in the 11 subjects significantly increased. The NE, ET-I, fasting INS, and HOMA-IR levels significantly decreased. The main indexes of body composition and biochemistry also changed significantly. Conclusion: Through this case study, we verified that Bigu can change the levels of serum vasoactive substances and major physiological/biochemical indicators, and decrease cardiovascular risk factors in sub-healthy women. Bigu is effective in preventing cardiovascular diseases in sub-healthy women.

Keywords: Bigu, serum vasoactive substances, primary prevention, cardiovascular diseases

Introduction

Cardiovascular diseases (CVDs) remain the leading cause of death worldwide, despite significant advances made in recent decades to understand the risk factors that contribute to CVDs [1]. The medication costs for prevention and treatment of CVDs continue to increase rapidly, causing severe burdens on the healthcare system and society. Therefore, simple and cheap treatments with vigorous non-pharmacologic therapy are needed to promote the prevention and treatment of CVDs [2].

"Bigu" is a Taoist term, which means to stop eating grains and cereals, that is food crops or cooked foods and at the same time practice vital energy (Qi) cultivation [3]. The practice of Bigu was passed down through generations to this day because the special effects of Bigu on in certain aspects of health, thus it has become a unique health-preserving skill of traditional Chinese medicine (TCM) over many centuries [4]. In modern times, Bigu practice has been improved and evolved from solo Bigu exercise to group Bigu practice involving multiple people [5]. Qi, a basic concept in ancient Chinese medicine, is an invisible, phaseless and ubiquitous energy, according to TCM theory [6]. During the normal living process, the body is mainly nourished by the diet and Qi. During the caloric restriction periods, the intake of food is artificially reduced or cut off, so the body will first utilize the reserved energy system. This process helps to purify the blood and treat a variety of different diseases [7]. However, once excess energy stores in the body are used during a fast, the body starts to use the essential energy-matter. Then, adverse effects will occur [8]. Though calorie restriction therapy affects various chronic diseases [9], its clinical use is limited by the adverse effects. "Fuqi" (acquiring Qi by Qigong exercise) can replace the diet-originated Qi with the innate Qi through Qigong practice, forming a new energy source in the

Table 1. Baseline characteristics of participants

Characteristic	Value (n=11)
Age (years)	50.6±10.78
Height (cm)	161.8±6.19
Body mass (kg)	64.9±9.10
BMI (kg/m^2)	24.8±3.42
BFM (kg)	23.0±7.31
SLM(kg)	39.5±3.91
Abdomen circumference (cm)	87.6±10.56
Waist-to-hip ratio	0.92±0.07
Percent body fat (%)	34.8±6.91

body [10]. Therefore, Fuqi by Qigong exercise should be intensified from the beginning of Bigu to complement the vital energy (Qi) in the body, which allows the practitioner to avoid the adverse reactions from calorie restriction. The above is exactly the principle of Bigu.

Bigu can strengthen physical health and prevent various chronic diseases according to ancient TCM literature [3-5, 10, 11]. We hypothesize that Bigu will change the serum vasoactive substances and some major physiological and biochemical indicators, as well as reduce cardiovascular risk factors and prevent CVDs in sub-healthy women according to our practical experience.

Material and methods

Subjects

Eleven sub-healthy Chinese women who felt unwell but had no clear disease index were selected from individuals who responded to the bulletins posted in hospitals and communities. The baseline characteristics of the subjects are shown in **Table 1**. They received Bigu training together. Serum vasoactive substances, body composition and major biochemical indicators were detected at the beginning and end of the Bigu training. All subjects were informed about and signed the right of informed consent. This trial was approved by the Medical Ethics Committee of NingXia Medical University (NXMU) (No. 2018-027), and the clinical trials were registered in the Chinese Clinical Trial Registry (No. ChiCTR1800016923).

The inclusion criteria were as follows: (1) 18 to 65 years of age; (2) no dementia or memory disorder; (3) no nerve, muscle and other physical diseases that affect normal practice; normal actions; (4) devotion of 7 days to Bigu exercises; (5) self-feeling of physical discomfort, but normal clinical test indicators, and no need of long-term medication.

The exclusion criteria were as follows: (1) no serious disease that required clinical observation or prohibited Bigu exercise; (2) xenogenic transplant or heart scaffold that was not suitable for practicing Bigu exercises.

The elimination criteria were as follows: (1) subjects who felt extremely hungry or needed extra food; (2) spontaneous study withdrawal for any reason.

Bigu intervention methods

Doctor Li Baoyou formulated the technical process of Bigu according to his family inheritance and TCM classics. We standardized the technical process and published it in the book "Bigu Health Preserving Practice [12]" on basis of abundant practical experience. During the 7-day Bigu intervention, the subjects participated in group Qigong practice in the morning, at noon, and in the evening. Each exercise lasted 1.5 to 2 hours and was supplemented with a 30-minute to 50-minute explanation of Qigong methods. The practitioners individually chose the little-eating or no-eating status according to their feelings. The Qigong skills for Bigu included dynamic Qigong, spontaneous dynamic Qigong, static Qigong, and walking Qigong. The Qigong exercises are listed in **Table 2**. Walking Qigong was practiced independently after collective exercises. Gentle classic music and spoken guidance helped the practitioners enter the Qigong state. During the Bigu period, the practitioners only drank spring water or were free to have fruit depending on their own conditions. At noon or night on the 7th day, they began to resume normal eating.

Outcome measures

Serum vasoactive substances and homeostatic model assessment of insulin resistance (HOMA-IR): In the morning of the 1st and 7th day, peripheral venous blood was collected from the fasting participants and placed into heparin anticoagulant tubes, which were centrifuged at 3000 rpm for 5 minutes. The serum

Table 2. Composition of the Bigu Qigong

Methods	Stage	Movement	Time
Spontaneous dynamic Qigong	Preparation	Stand naturally, put feet shoulder-width apart on parallel lines, bend knees slightly, bow hands naturally, and put head straight.	2 min
	Movement	Stand still naturally. Relax the mind and body gradually. Move spontaneously; or wiggling of feet or body is acceptable as the practice proceeds.	20 min
	End	Fold both hands and place them on the abdomen, use a mind to end the practice; then and pat the appointed acupoints.	5 min
dynamic Qigong	Preparation	Adduct toes slightly; the other postures are the same as spontaneous dynamic Qigong.	2 min
	First part	Stand still naturally, and use a mind to open the whole body's pores and breathe with them.	5 min
	Second part	Stand still naturally and put the palms together on the chest. Use mind to let coloured light enter the body, to form a baihui point on the head top and to irradiate the internal organs.	5 min
	Third part	Stand still naturally, with a lotus fingerprint on the chest. Recite five different sounds and feel the vibration of the internal organs.	5 min
	Fourth part	Stand still naturally, with both hands opening and closing in front of the chest, the eyes, and the navel. Notice how your body feels.	5 min
	End	The same as spontaneous dynamic Qigong	5 min
Static Qigong	Preparation	Sit upright on a chair, with head straight and hands flat on both legs; or sit cross-legged on a cushion.	2 min
	Movement	Keep the posture constant and gradually relax. Spontaneous body wiggling is acceptable.	20 min
	End	The same as spontaneous dynamic Qigong.	5 min
Walking Qigong	Preparation	Choose a safe and quiet environment.	
	Movement	Walk slowly and gradually relax the body. Remain quiet without speaking.	At will
	End	Fold both hands and place them on the abdomen; use a mind to end the practice.	1 min

was separated and stored at -80°C. The serum levels of fasting insulin (FINS), norepinephrine (NE), endothelial nitrogen monoxide synthase (eNOS), endothelin-I (ET-I), and angiotensin-II (Ang-II) were measured by using enzyme-linked immunosorbent assay (ELISA) kits according to the manual on a Multiskan MK3 automatic microplate reader (Thermo scientific). The kits (all from Elabscience, China) included human insulin ELISA kits (E-EL-H5439c), norepinephrine ELISA kits (E-EL-0047c), human endothelial nitric oxide synthase ELISA kits (E-EL-H0755c), human endothelin-I ELISA kits (E-EL-H0064c), and human angiotensin II ELISA kits (E-EL-H0326c). HOMA-IR, an index of insulin resistance, was calculated as follows: [fasting glucose (mmol/L) × fasting insulin (mU/L)]/22.5 [13].

Diet and water intake: The type and amount of daily food intake (mainly fruit) and water intake were all recorded from the 11 subjects for measurement of daily energy intake.

Body composition: Body composition parameters were examined using a body composition analyzer (InBody 770) for direct segmental multi-frequency bioelectrical impedance analysis. The parameters included body weight, body mass index (BMI), soft lean mass (SLM), body fat mass (BFM), waist-to-hip ratio (WHR), basal metabolic rate (BMR), total body water (TBW), intracellular water (ICW), extracellular water (ECW), and protein level.

Basic biochemical indicators: The serum samples obtained in the morning of the 1st and 7th days were partially separated. Major biochemical indicators were measured on an Olympus AU400 biochemical auto-analyzer. The blood lipid indicators included cholesterol (CHOL), triglyceride (TG), high-density lipoprotein (HDL), and low-density lipoprotein (LDL). Other primary biochemical indicators were fasting blood glucose (FBG), glutamic-pyruvic transaminase (ALT), glutamic-oxalacetic transaminase (AST), total bilirubin (TBIL), direct bilirubin (DBIL), indirect bilirubin (IBIL), total protein (TP), albumin (ALB), globulin (GLB), phosphatase (ALP), transaminase (GPT), urease (Ure), creatinine (CRE), uric acid (UA), and creatine kinase (CK).

Sample size: We actively recruited and finally enrolled eleven sub-healthy women. All available subjects during this period who met all the eligibility criteria were included in this study.

Statistical analysis: We performed all statistical analyses using SPSS v.22.0 software. Measurement data were presented as mean ± standard deviation and difference tests were using Paired sample t-test. Significance level set as α=0.05.

Results

Completion of Bigu

Bigu practice was carried out under the leadership of Dr. Li Baoyou and his team. The 11 participants all took part in group Qigong practice and stopped eating during the 7-day Bigu period. On each day, the participants completed 4 to 5 hours of Qigong exercises. Between the 2nd and 5th days, some of the participants felt slight fatigue, which lasted for 1-3 days. The fingertip blood glucose levels taken during the Bigu period were within normal range. The daily calorie intake of the 11 participants from the 2nd to the 6th day was 28 to 475 kcal from various fruits, and the daily water intake was 1000 to 2000 mL.

Effects of Bigu on serum vasoactive substances

Compared with the first day of Bigu practice, the eNOS (P<0.01) levels increased significantly on the 7th day, whereas the NE (P<0.01), ET-I (P<0.05), FINS (P<0.05) levels and HOMA-IR (P<0.01) all significantly decreased (**Table 3**; **Figure 1**). ANG-II levels also decreased, but not significantly.

Effects of Bigu on body composition

Compared with the first day of Bigu practice, the weight, BMI, and levels of SLM, BMR, TBW, ICW, ECW, and protein significantly decreased (all P<0.01) on the 7th day, but no significant difference was found in the level of BFM or WHR (**Table 4**).

Effects of Bigu on major biochemical indices

On the 7th day of Bigu compared with the first day, the level of TG significantly decreased (P<0.05), but the levels of TCHO, HDL, and HDL did not significantly differ (**Table 5**). The levels

Table 3. Bigu on level of serum vasoactive substances and HOMA-IR on the 1st day vs. the 7th day (n=11, x ± s)

Time	eNOS (pg/mL)	ET-I (ng/mL)	Ang-II (pg/mL)	NE (ng/mL)	FINS (μU/mL)	FBG (mmol/L)	HOMA-IR units
The 1st Day	7574.91±4115.72	3.07±1.76	122.22±54.55	1.46±0.90	0.84±0.29	5.29±0.67	0.19±0.06
The 7st Day	13354.88±5917.09**	2.69±2.10*	111.57±48.38	1.26±0.88**	0.68±0.21*	4.98±0.61*	0.15±0.05**
t	-4.425	2.743	1.462	4.176	3.062	2.265	3.617
p	0.001	0.021	0.174	0.001	0.012	0.047	0.005

*Significantly different on the 1st day vs. the 7th day (P<0.05); **very significantly different on the 1st day vs. the 7th day (P<0.01).

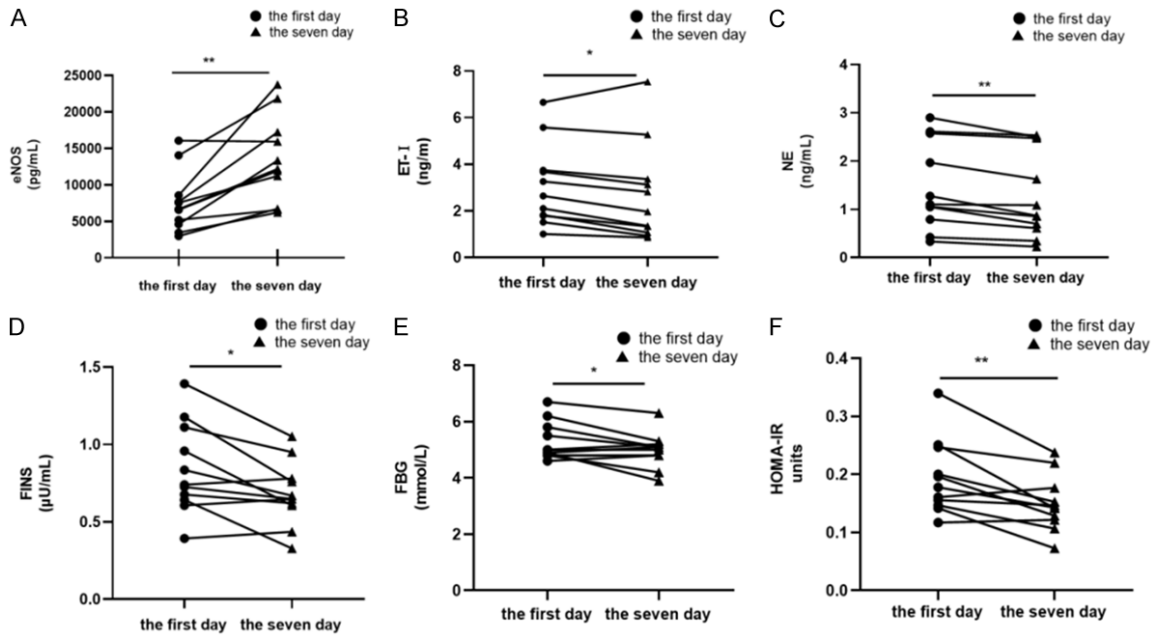

Figure 1. Compared with the 1st day and the 7th day. A: eNOS; B: ET-I; C: NE; D: FINS; E: FBG; F: HOMA-IR. Compared with the 1st day and the 7th day. *P<0.05, Significantly different on the 1st day vs. the 7th day. **P<0.01, Very significantly different on the 1st day vs. the 7th day (n=11).

of AST and DBIL significantly increased (both P<0.01), but the levels of ALT, TBIL, IBIL, ALP, and GPT did not significantly change (**Table 6**). The levels of URE (P<0.05), CRE (P<0.05), UA (P<0.01) and CK (P<0.05) all significantly increased, but no significant difference was found in the levels of TP, ALB or GLB (**Table 7**).

Discussion

Vascular endothelial cells (VECs) are flat squamous cells that continuously cover the inner surface of blood vessels. VECs are an important barrier between blood and vascular walls, and can secrete various vasoactive substances. Thus, VECs are pivotal in regulating vascular tension and maintaining balance among blood metabolites. Vascular endothelial dysfunction is an independent predictor of cardiovascular diseases and can occur in the aorta, renal artery and other large blood vessels [14]. Our experiments prove that Bigu can significantly regulate the endothelial functions and help prevent CVDs of sub-healthy women.

The improvement effect of Bigu on endothelial functions of sub-healthy women

NO is an important vascular dilating factor secreted in endothelial cells. The endothelial nitric oxide synthase (eNOS), a rate-limiting enzyme of induced NO synthesis, can protect the cardiovascular system and prolong life [15]. In our experiments, the serum eNOS levels in the 11 sub-health adult females were 7574.91±4115.72 pg/mL before Bigu practice (n=11), and rose significantly to 13354.88± 5917.09 pg/mL after Bigu practice (P<0.01, n=11). Of them, the eNOS level in one 51-year-old participant rose from 8,565.47 pg/mL by

Table 4. Bigu on level of body composition on the 1st day vs. the 7th day (n=11, x ± s)

Time	Weight (kg)	BMI (kg/m^2)	BFM (kg)	SLM (kg)	WHR	BMR (kcal)	Protein (kg)	TBW (L)	ICW (L)	ECW (L)
The 1st Day	64.89±9.10	24.79±3.42	22.99±7.31	39.47±3.91	0.9155±0.071	1275.3±89.31	8.15±0.25	30.81±3.04	18.89±1.82	11.87±1.22
The 7st Day	62.49±8.53**	23.89±3.25**	22.66±7.22	37.53±3.56**	0.9218±0.062	1230.36±82.66**	7.82±0.22**	29.25±2.79**	18.05±1.70**	11.19±1.11**
t	6.329	5.923	1.544	4.777	-0.635	4.836	4.425	4.777±	5.239	4.104
p	<0.001	<0.001	0.154	0.001	0.540	0.001	0.001	0.001	<0.001	0.002

**Very significantly different on the 1st day vs. the 7th day (*P*<0.01).

Table 5. Bigu on level of blood lipids on the 1st day vs. the 7th day (n=11, x ± s)

Time	TCHO (mmol/L)	TG (mmol/L)	HDL (mmol/L)	LDL (mmol/L)
The 1st Day	4.46±0.74	1.65±0.89	1.32±0.20	2.87±0.54
The 7st Day	4.38±1.00	1.10±0.36*	1.28±0.22	3.04±0.83
t	0.422	2.809	0.932	-1.020
p	0.682	0.019	0.373	0.322

*Significantly different on the 1st day vs. the 7th day (P<0.05).

nearly 3 times to 23,733.07 pg/mL after Bigu practice. ET is one of the effective vasoconstrictor substances. ET-I molecules are mainly expressed in VECs, and the expression levels affect the occurrence and development of many cadio-cerebrovascular diseases [16]. In our experiments, the serum ET-I levels dropped significantly from 3.07±1.76 ng/mL before Bigu practice to 2.69±2.10 ng/mL after practice (P<0.05, n=11). These results indicate Bigu can significantly improve the functions of endothelial cells in vivo, but the underlying mechanism is worth further exploration.

Probable action mechanism of Bigu on endodermial functions

The activity of the sympathetic nervous system can affect the function of endothelial cells. NE is a transmitter for many systems and is directly related to its excitability [17]. The serum NE levels dropped significantly from 1.46±0.90 ng/ml before Bigu practice to 1.26±0.88 ng/mL after practice (P<0.01, n=11), suggesting Bigu may reduce the excitability of the sympathetic nervous system, which may be because Bigu can improve the function of endothelial cells. The renin-angiotensin system can significantly regulate the function of endothelial cells. Ang-II is a main active peptide in the renin-angiotensin system, and can critically modulate blood pressure [18]. The Ang-II levels dropped from 122.22±54.55 pg/mL before Bigu practice to 111.57±48.38 pg/mL after practice (n=11), but not significantly, indicating the renin-angiotensin system may not be a major route of endothelial function regulation during Bigu practice. Oxidative stress is a major cause for the decline of endothelial function. Bilirubin, one of the two endogenous antioxidants *in vivo*, has antioxidation, immunomodulatory, cerebral nerve-protection, as well as anti-inflammatory and pro-cardiovascular effects on the body when it is at certain concentrations. Reportedly, appropriate rise of bilirubin levels is a main cause for the improvement of endothelial function [19]. The bilirubin levels significantly rose within appropriate range after the Bigu practice, which is consistent with a previous study [20].

Effects of Bigu on basic physiological and biochemical indicators

Body component analysis showed the body mass and body mass index significantly decreased after multiple days of Bigu diet restriction, and the protein level, soft lean mass, and body fat mass all declined slowly, but the reductions were all within appropriate ranges, without sudden reduction. The total water content of cells, intracellular water content, and extracellular water content all declined appropriately during the Bigu period, but no unbalance between intracellular liquids and extracellular liquids, and no evident dehydration or edema caused by hunger occurred. Body component analysis demonstrated multiple days of Bigu practice did not cause excessive physiological discomfort.

Due to the lack of exogenous energy during the Bigu diet restriction, the muscle mass decreased, and the creatinine content due to muscle degradation increased, so the serum creatinine contents rose appropriately. The serum creatinine level increased from 64.27± 5.96 μmol/L before Bigu to 69.49±7.40 μmol/L after Bigu (P<0.01, n=11), which did not exceed the normal clinical range, indicating the renal functions were not severely affected. Bigu diet restriction drove the body to decompose abundant aged cells to provide energy. The nucleic acids in the aged cells were decomposed to purines, which raised the serum uric acid level. Moreover, the increase in energy utilization also led to a rise of serum creatine kinase concentration. The increase in the metabolite concentrations intensified the metabolic pressure of liver cells, leading to appropriate rise in the levels of AST and ALT. Nevertheless, the rise of these indices was all within physiological ranges. Reportedly, after one month of diet recovery, the changes in these indices will return to the levels before Bigu practice, and are only temporary and transient [21].

Table 6. Effects of Bigu on major liver function indices on the 1st day vs. the 7th day (n=11, x ± s)

Time	ALT (U/L)	AST (U/L)	TBIL (μmol/L)	DBIL (μmol/L)	IBIL (μmol/L)	ALP (U/L)	GPT (U/L)
The 1st Day	20.75±7.66	21.84±4.52	11.70±3.90	2.37±0.94	9.33±3.03	87.45±17.89	20.97±10.10
The 7st Day	28.71±13.46	29.27±5.87**	14.55±5.85	3.32±0.94**	11.31±4.07	88.18±19.92	20.64±11.59
t	-1.885	-4.117	-2.196	-3.619	-1.806	-0.292	0.345
p	0.089	0.002	0.053	0.005	0.101	0.776	0.738

**very significantly different on the 1st day vs. the 7th day (*P*<0.01).

Table 7. Effects of Bigu on major renal function indices on the 1st day vs. the 7th day (n=11, x ± s)

Time	URE (mmol/L)	CRE (μmol/L)	UA (μmol/L)	CK (μmol/L)	TP (g/L)	ALB (g/L)	GLB (g/L)
The 1st Day	4.53±1.04	64.27±5.96	284.68±57.67	92.15±21.93	71.40±4.40	44.85±3.99	26.55±3.07
The 7st Day	3.70±0.99*	69.49±7.40**	356.43±70.81*	126.05±49.68*	73.47±3.76	46.24±2.40	27.24±3.79
t	2.361	-3.337	-2.370	-3.026	-1.154	-1.320	-0.794
p	0.040	0.008	0.039	0.013	0.275	0.216	0.446

*Significantly different on the 1st day vs. the 7th day (*P*<0.05); **very significantly different on the 1st day vs. the 7th day (*P*<0.01).

In all, body component analysis and biochemical indicator detection prove that Bigu diet restriction under professional and scientific instruction is safe and will not cause sudden decline in muscle mass and protein content due to excessive hunger, or dehydration or edema, nor long-term adverse effects on biochemical indicators. Bigu can significantly improve the serum eNOS levels of participants, decrease serum ET-I levels, and significantly enhance the endothelial cell functions *in vivo*. Bigu can improve the function of endothelial cells and Bigu can also significantly decrease physiologic indices (e.g. body mass, BMI, BFM, and BMR) and biochemical indicators (e.g. TG, FBG, FINS levels). These are all important factors affecting the occurrence and development of CVDs. Thus, Bigu may have critical values in preventing cardiovascular diseases among sub-healthy people. In the future, we will collect more data in projects with Bigu intervention of cardiovascular diseases, and observe the effects of Bigu on the risk factors of cardiovascular diseases in metabolic syndrome patients. We will also summarize our guidelines and theoretically explain the clinical application of Bigu.

Conclusions

Bigu is a therapy that has not been applied in clinic practice on large scales. This case report presents the potential usefulness of non-pharmacologic prevention for CVDs. CVDs remain the leading cause of death worldwide, and Bigu may help prevent CVDs. Bigu is therefore a potential option to be incorporated into a larger study on primary prevention of CVDs.

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Disclosure of conflict of interest

None.

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