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Original Article
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Interactive Effects of Nutrition Modification and Wet Cupping on Male Patients with Refractory Stable Angina

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Objectives: Routine therapies cannot control refractory stable angina, leading to a high economic burden and an impaired quality of life. Persian medicine incorporates exceptional attention to lifestyle and nutrition to prevent and treat various diseases. Previous studies have reported the analgesic and anti-inflammatory effects of wet cupping. The present study aims to determine the effects of nutrition and cupping on refractory stable angina patients.

Methods: Forty male patients with refractory stable angina were randomly allocated to four groups, including nutrition modification based on Persian medicine, wet cupping, nutrition modification along with wet cupping, and control. The primary outcomes were the changes in pain score using a visual analog scale and quality of life using the Seattle angina questionnaire. The secondary outcomes were changes in the exercise test and blood pressure.

Results: The results of the present study revealed that 30 days of treatment with nutrition modification based on Persian medicine, cupping, and modified nutrition and cupping along with standard treatment for stable angina significantly increased the patient's quality of life and exercise test results while reducing pain, and systolic and diastolic blood pressure.

Conclusion: Applying complementary Persian medicine methods such as nutrition modification and cupping along with the classical medical treatments may improve outcomes for refractory stable angina patients.

Keywords: wet cupping, nutrition, persian medicine, refractory stable angina

INTRODUCTION

Cardiovascular diseases are considered one of the most widespread and severe complications in various societies and are increasingly growing in recent decades [1]. Stable angina, the most experienced disorder among cardiovascular events, is a clinical attack syndrome caused by transient myocardial ischemia [2]. Additionally, refractory angina is characterized by angina that cannot be controlled by routine medical therapies and revascularisation methods. Patients with refractory angina experience a significantly impaired quality of life along with a high burden and utilization of healthcare services [3].

Nowadays, complementary and alternative medicine (CAM) is becoming more popular with the public and is gaining credibility within the biomedical health care communities [4, 5]. CAM incorporates lifestyle, nutrition, and special treatments such as cupping and phlebotomy to prevent and treat several disorders, in a manner that is less complicated, more economic,

and effective [6, 7].

Cupping is a technique that involves creating negative pressure and a vacuum over the skin at specific points using cups and can be performed by dry or wet cupping [8]. Previous clinical studies have shown that wet cupping might exert analgesic and anti-inflammatory effects by releasing β-endorphin and adrenocortical hormone into the circulation following skin injury [9]. Furthermore, it has been shown that cupping diminished high-sensitivity C-reactive protein (hs-CRP) levels, which is clinically important in the progression and improvement of coronary artery disease [10, 11].

The present study aimed to determine nutrition modification and cupping effects on patients with refractory stable angina.

MATERIALS AND METHODS

1. Ethics

This study was confirmed by the ethics committee of Mashhad University of Medical Sciences (approval code. IR.MUMS.REC.1396.227). Furthermore, this trial was registered at https://www.irct.ir/ (No. IRCT20171004036564N1). All participants received and signed written informed consent.

2. Study design and randomization

This study was a randomized, controlled, open-label trial on male patients between the ages of 18-70 years diagnosed with refractory stable angina and referred to the cardiovascular clinic in Imam Reza Hospital of Mashhad University of Medical Sciences. Participants were excluded if they had bleeding susceptibility, active thrombophlebitis, and BMI < 15 or > 35 kg/m^2. After enrolment, patients were randomly assigned into four groups:

A: Standard treatment + nutrition correction

B: Standard treatment + cupping (twice during the study: at the beginning and day 30)

C: Standard treatment + cupping + nutrition correction

D: Standard treatment

Table 1. Diet plan

Meal	Foods
Breakfast	- Mung beans or beans with two loaves of bread - Low fat unsalted cheese - Fresh yoghurt with mint - One egg yolk - Apple, carrot, pineapple, and barberry jams - Almonds, beets and turnips
Lunch	- Barley soup containing barley, coriander, mung bean, lettuce and zucchini - Ashshole containing spinach, mung bean, pomegranate juice, flour, purslane - Zucchini feed - Fish - Chicken meat - Sheep meat - Chicken soup containing chicken meat, chickpeas, vegetables such as spinach, and coriander with rice
Dinner	- Pumpkin feed and pomegranate juice - Barberry feed with almonds - Peas with mustard and olive oil - Fewer amounts of foods listed as lunch
Snack	- Snacks: dried berries, figs - Fruits: mango, pineapple, pomegranate, figs, apple, cucumber, blackberry - Salads containing cabbage, lettuce, cucumber, carrot, and tomato with lemon or orange juice - Herbal tea: apple, berries, coriander, and cinnamon
Abstinence	- Overeating or starvation - Drinking cold water - Creamy pastries, baguette bread, pasta, and fast food - Alcoholic beverages

3. Diet plan

Foods beneficial for the heart and for refractory stable angina were obtained from traditional Persian resources, including the Canon of Medicine (Avicenna, 1025 AD) [12], Al-Hawi Fi Tibb [13], and Teb e Akbari [14]. After that, a dietary regimen was designed based on the selected foods, considering the patient's eating habits and availability of ingredients (Table 1). In addition, according to Persian medicine concepts, patients were free to choose the type and quantity of foods listed in our recommended list according to their appetite.

4. Cupping method

Cupping was applied using plastic disposable vacuum cups in five areas, including T2-T4 on the back of the thoracic spine and the 2nd, 3rd, 4th, and 5th intercostal space in the front of the left chest for 5 minutes (Fig. 1). Bloodletting was done only in the T2-T4 back areas.

5. Evaluation of outcome

Exercise testing, systolic (SBP) and diastolic (DBP) blood pressure, the Seattle angina questionnaire (SAQ), and the pain measurement instrument of the visual analog scale (VAS) were performed at the beginning of the study and after 30 days of intervention.

6. Estimation of sample size

Due to a lack of previous similar studies and difficulty finding patients during the COVID-19 pandemic, this study was designed as a phase 2 pilot clinical trial investigating the safety and effectiveness of the interventions. Therefore, the sample size of this study was estimated as 10 patients in each group, for a total of 40 patients.

7. Statistical analysis

SPSS version 16 (SPSS Inc., Chicago, Illinois) was used for statistical analyses. Variables with a normal distribution were expressed as mean ± standard deviation (SD). They were analyzed using ANOVA and Tukey *post hoc* tests to calculate the differences between the groups and a paired t-test for before and after comparisons. The differences between non-normal variables were determined using Kruskal-Wallis or Mann-Whitney tests, and before and after comparisons in each group were performed using the Wilcoxon test.

RESULTS

1. Study population and clinical characteristics between the four groups

In this study, 90 patients with refractory stable angina were initially referred, 40 of which were not eligible, and 10 were excluded. Thus, a total of 40 patients were enrolled and successfully completed the study (Fig. 2). The patients' demographic characteristics were well distributed between the four groups (Table 2).

2. The effects of cupping and nutrition modification on exercise testing

At the end of the 30 days of the study, the exercise test results in the cupping and nutrition modification groups were notably

Figure 1. The location and manner of cupping.

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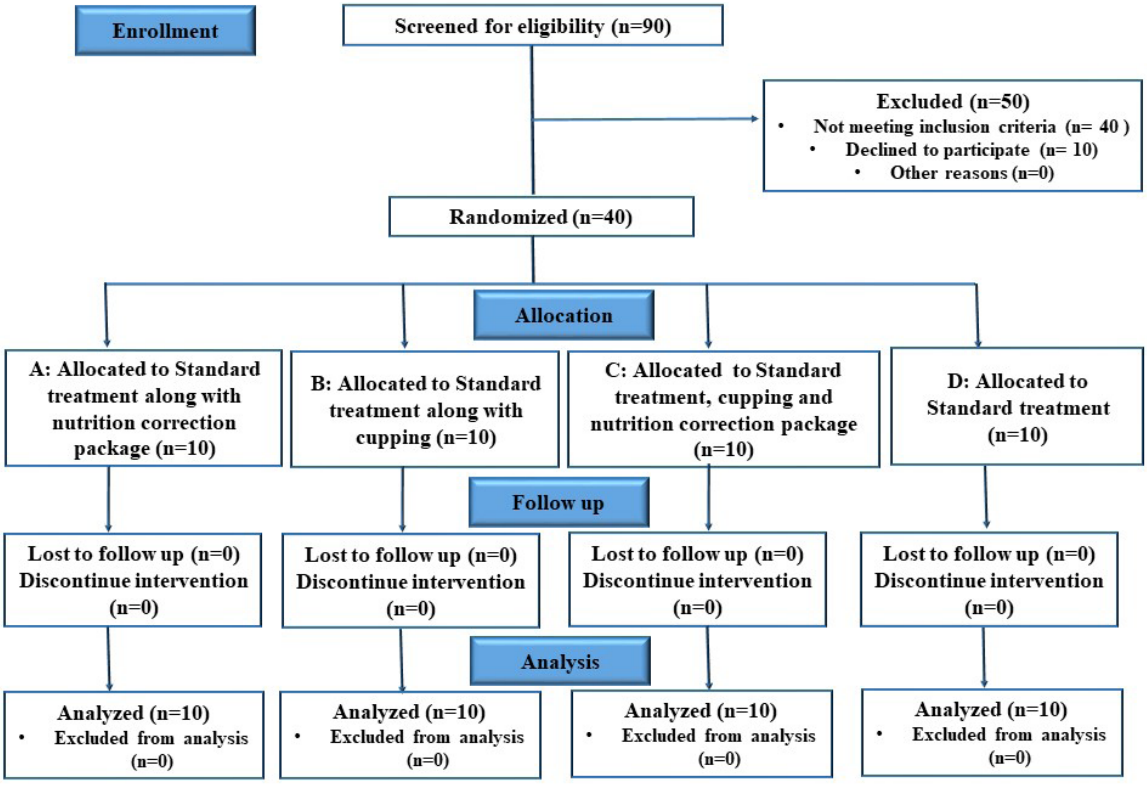

Figure 2. The study flowchart.

Table 2. Participants' demographic information

Mean ± SD or N (%)	Group				p-value
	A	B	C	D	
Age (years)	56.60 ± 9.5	49.40 ± 6.99	52.3 ± 7.24	54.40 ± 9.6	0.28
BMI (kg/m^2)	25.60 ± 3.55	24.40 ± 3.85	26.13 ± 2.63	25.52 ± 2.49	0.68
Duration of disease					0.54
< 5 years	3 (30.0)	4 (40.0)	4 (40.0)	1 (10.0)	
6-10 years	2 (20.0)	3 (30.0)	3 (30.0)	6 (60.0)	
> 10 years	5 (50.0)	3 (30.0)	3 (30.0)	3 (30.0)	
Angioplasty					0.24
1-5	8 (80)	5 (50)	4 (40)	9 (90)	
6-10	1 (10)	2 (20)	3 (30)	0 (00)	
> 10	1 (10)	3 (30)	3 (30)	1 (10)	
CABG					0.88
Yes	3 (30.0)	3 (30.0)	5 (50.0)	4 (40.0)	
No	7 (70.0)	7 (70.0)	5 (50.0)	6 (60.0)	

increased compared to the control group ($p < 0.001$ for both cases, Table 3). Furthermore, there was a significant change in levels in the exercise test in all three treated groups compared to the control group ($p < 0.001$ for all cases). In addition, all three interventions meaningfully enhanced the exercise test results compared to their baseline results ($p < 0.001$ for all cases, Table 3).

Table 3. The exercise test results before (day 0) and after (day 30) treatment

Exercise test (Mean ± SD)	Group				p-value[a]
	A	B	C	D	
Baseline	11.0 ± 4.54	8.40 ± 4.99	11.80 ± 4.98	14.30 ± 6.0	0.1
End	17.60 ± 2.63	16.66 ± 4.53	20.30 ± 2.83***	12.80 ± 6.24	0.004
Discord	↑6.60 ± 4.24***	↑8.20 ± 4.69***	↑8.50 ± 4.69***	↓1.5 ± 5.02	< 0.001
p-value[b]	0.001	0.001	0.001	0.38	-

↑: Increment, ↓: Decrement; ***p < 0.001 comparing the mentioned group and its control group, [a]results of ANOVA test between four groups, [b]results of paired t-test comparison before and after the treatment.

Table 4. The SBP and DBP results before (day 0) and after (day 30) treatment

mmHg; Mean ± SD	Group				p-value[a]
	A	B	C	D	
SBP					
Baseline	129.6 ± 18.055	130.9 ± 14.95	133.20 ± 15.06	119.40 ± 15.54	0.24
End	123.0 ± 16.85	123.0 ± 12.81	116.80 ± 15.50	126.0 ± 14.68	0.56
Discord	↓9.30 ± 12.69*	↓14.10 ± 14.98***	↓9.90 ± 7.39	↑6.60 ± 8.57	0.002
p-value[b]	0.06	0.01	0.002	0.04	-
DBP					
Baseline	79.70 ± 11.80	84.30 ± 10.40	79.30 ± 7.0	78.10 ± 10.24	0.54
End	71.60 ± 8.03*	72.20 ± 8.96	74.90 ± 8.69	81.50 ± 6.95	0.04
Discord	↓8.10 ± 6.78**	↓12.10 ± 7.50***	↓4.40 ± 7.50	↑3.40 ± 7.69	0.001
p-value[b]	0.004	0.001	0.1	0.19	-

↑: Increment, ↓: Decrement; *p < 0.05, **p < 0.01, and ***p < 0.001 comparing the mentioned group and its control group, [a]results of ANOVA test between four groups, [b]results of paired-t-test before and after the treatment.

3. The effects of cupping and nutrition modification on SBP and DBP

The nutrition modification and cupping groups had a significantly decreased SBP compared to the control group ($p < 0.05$ and $p < 0.001$, respectively). Additionally, the cupping along with nutrition modification ($p = 0.002$) and cupping ($p = 0.01$) groups had a remarkably reduced SBP at the end of the 30 days compared to their baseline (Table 4).

The present study results revealed that 30 days of treatment with all three interventions attenuated the DBP compared to the control group; however, only the effect of nutrition modification was statistically significant ($p < 0.05$). Moreover, the changes in DBP were more remarkable in the nutrition modification ($p < 0.01$) and cupping ($p < 0.001$) groups than in the control group. In addition, the nutrition modification ($p = 0.04$) and cupping ($p = 0.001$) groups considerably mitigated their DBP compared to baseline levels (Table 4).

4. The effects of cupping and nutrition modification on Seattle angina questionnaire scores

The results revealed that all three groups markedly promoted physical limitations, angina stability, angina frequency, treatment satisfaction, and disease perception scores compared to the control group ($p < 0.001$ for all cases, Table 5). Moreover, all three intervention groups significantly elevated the physical limitations, angina stability, angina frequency, treatment satisfaction, and disease perception scores compared to their respective baseline scores ($p < 0.001$ for all cases, Table 5).

5. The effects of cupping and nutrition modification on pain intensity

All three intervention groups strikingly alleviated the pain score following one, two, and three months of intervention compared to the control group ($p < 0.001$ for all cases, Table 6).

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Table 5. The SAQ results before (day 0) and after (day 30) treatment

Mean ± SD	Group				p-value[a]
	A	B	C	D	
Physical limitation					
Baseline	20.30 ± 2.49	20.0 ± 6.14	20.80 ± 5.24	25.40 ± 3.24	0.04
End	35.20 ± 4.96***	36.80 ± 2.48***	37.0 ± 4.61***	23.70 ± 5.01	< 0.001
Discord	↑14.90 ± 6.75***	↑16.80 ± 8.11***	↑16.20 ± 5.97***	1.7 ± 4.62	< 0.001
p-value[b]	0.001	0.001	0.001	0.28	-
Angina stability					
Baseline	2.70 ± 1.33	2.0 ± 1.15	2.30 ± 0.94	4.0 ± 0.66	0.001
End	5.40 ± 0.96	5.40 ± 0.69	5.30 ± 0.82	4.30 ± 1.82	0.11
Discord	↑2.70 ± 0.95***	↑3.40 ± 0.96***	↑3.0 ± 0.97***	↑0.30 ± 2.32	< 0.001
p-value[b]	0.001	0.001	0.001	0.68	-
Angina frequency					
Baseline	5.0 ± 1.88	4.30 ± 2.54	4.40 ±2.06	8.0 ± 2.44	0.002
End	10.70 ± 1.25*	10.1 ± 1.52	10.0 ± 0.66	8.4 ± 2.59	0.02
Discord	↑5.70 ± 1.70***	↑5.8 ± 0.96***	↑5.60 ± 2.12***	↑0.40 ± 3.80	< 0.001
p-value[b]	0.001	0.001	0.001	0.74	-
Treatment satisfaction					
Baseline	8.40 ± 1.98	7.10 ± 2.55	7.30 ± 2.31	8.70 ± 2.0	0.30
End	18.70 ± 2.98***	18.80 ± 1.8***	7.40 ± 1.83***	12.20 ± 4.10	< 0.001
Discord	↑10.30 ± 3.50***	↑11.70 ± 3.71***	↑4.40 ± 1.77***	↑3.50 ± 5.20	< 0.001
p-value[b]	0.001	0.001	0.001	0.07	-
Disease perception					
Baseline	2.90 ± 0.87	2.30 ± 0.65	3.0 ± 1.94	2.9 ± 1.3	0.63
End	7.90 ± 1.10***	6.80 ± 1.3***	7.40 ± 1.83***	3.9 ± 2.51	< 0.001
Discord	↑5.0 ± 1.56***	↑4.50 ± 0.97***	↑4.40 ± 1.77***	↑1.0 ± 2.54	< 0.001
p-value[b]	0.001	0.001	0.001	0.001	-

↑: Increment, *p < 0.05 and ***p < 0.001 comparing the mentioned group and its control group, [a]results of ANOVA test between four groups, [b]results of paired-t-test before and after the treatment.

Table 6. The VAS results before (day 0) and after the first, second, and third months of treatment

Mean ± SD	Group				p-value[a]
	A	B	C	D	
Baseline	8.6 ± 0.96	8.1 ± 1.28	8.0 ± 0.94	5.3 ± 2.62	< 0.001
First	3.4 ± 1.64***	3.7 ± 2.66***	3.3 ± 2.71***	6.5 ± 1.77	< 0.001
Second	1.9 ± 1.1***	2.1 ± 1.65***	1.9 ± 1.37***	7.0 ± 1.63	< 0.001
Third	1.3 ± 2.75***	1.0 ± 1.84***	0.4 ± 0.52***	7.0 ± 1.88	< 0.001
Discord	↓7.3 ± 2.8***	↓7.1 ± 2.28***	↓7.6 ± 0.84***	↑1.7 ± 3.43	< 0.001
p-value[b]	< 0.001	< 0.001	< 0.001	0.12	-

↑: Increment, ↓: Decrement; ***p < 0.001 comparing the mentioned group and its control group, [a]results of ANOVA test between four groups, [b]repeated measurements ANOVA results in each group before and after the first, second, and third months of treatment.

Furthermore, before and after comparisons showed a significant decrease in pain scores following the one, two, and three months of treatment with all three interventions compared to their baseline ($p < 0.001$ for all cases). Interestingly, the pain score was elevated in the control group between the end of the third, second, and first months of the study; however, this was not statistically significant ($p = 0.12$, Table 6).

DISCUSSION

To the best of our knowledge, the current study is the first to determine the effects of wet cupping and nutrition modification based on Persian medicine in patients with refractory stable angina. The findings of this study indicated that 30 days of treatment with the modified diet, cupping, and modified nutrition and cupping along with standard treatment significantly increased the patient's quality of life and results of the exercise test while reducing the patient's pain, SBP, and DBP.

In the present study, we performed the SAQ and VAS scales to evaluate the quality of life and pain in refractory stable angina patients. All three intervention groups significantly decreased the SAQ and VAS scores following 30 days of treatment. Interestingly, the pain relief properties of cupping and nutrition modification lasted for two months after the cessation of treatment. In accordance with our results, wet cupping diminished the pain score measured by VAS and enhanced the quality of life in patients with migraine [15]. Similarly, wet cupping significantly improved the quality of life, including the physical, psychological, social, and environmental domains in patients with chronic medical conditions such as hypertension, diabetes, and neuropathy [16]. Additionally, dry cupping notably attenuated the hs-CRP levels, as an inflammatory marker, and pain measured by the VAS scale in women with chronic pelvic pain [17]. It has been emphasized that the analgesic mechanism of wet cupping is attributed to increased levels of nitric oxide in the region and increased local circulation [18]. Pain relief in patients receiving diet modification may be related to the anti-inflammatory, vasodilatory, and blood viscosity-reducing properties of dietary compounds such as apples [19] and peas [20].

The exercise test was performed on all patients before and after the intervention. Our results revealed that all three groups had enhanced exercise test results compared to the control group. In line with our results, cupping diminished the infarct size and the rate of ischemic-induced arrhythmias following myocardial ischemic reperfusion injury in male rats [21]. Similarly, wet cupping significantly attenuated the levels of interleukin-6 and tumor necrosis factor-α following the exercise-induced stimulation of inflammatory markers in male athletes [22]. In addition, the increase in test duration of the diet group may be attributed to the cardiotonic and vasodilatory properties of compounds such as barberry [23] and coriander [24].

The present study results also showed that all three intervention groups had notably alleviated their SBP and DBP. Interestingly, the blood-lowering properties of the cupping group were higher than the nutrition modification group. In accordance with our results, previous studies noticed that wet cupping remarkably mitigated SBP in patients with hypertension [25]. Additionally, wet and dry cupping reduced SBP, DBP, and pulse rate while enhancing oxygen saturation [26]. Furthermore, previous studies supported the blood-lowering effects of several natural compounds, including barberry [27] and pomegranate juice [28].

LIMITATIONS

Our study has some limitations. It was almost impossible to blind patients and investigators due to the type of interventions. Another limitation of our study is that we could not enroll women with refractory stable angina due to the heterogeneity of their menstrual cycle and their hormone protection (estrogen). Furthermore, our study was the first of its kind and will be considered a pilot study for future evaluations. Therefore, we included male patients with refractory stable angina in the current exploration. We firmly suggest that further investigation is required, particularly in female patients with refractory stable angina, to support and provide better insight into the effectiveness of nutrition modification and wet cupping against refractory stable angina.

CONCLUSION

Our results support that nutrition modification based on Persian medicine and cupping, alone or together in combination, ameliorated the pain score and blood pressure while increasing the quality of life and results of the exercise test in patients with refractory stable angina. Therefore, it is recommended to perform complementary medicine methods in addition to the classical medical therapies to achieve an appropriate therapeutic response. However, further studies with a larger number of patients are required to confirm our findings.

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CONFLICT OF INTEREST

The authors declare that there are no conflicts of interests.

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