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ORIGINAL ARTICLE

Impact of Ramadan Fasting on Biochemical and Exercise Parameters Among Patients Undergoing Exercise-Based Cardiac Rehabilitation

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Abstract

Background: **Ramadan fasting is an important worship activity for Muslims. It is not known if fasting could have deleterious effect on cardiac patients joining cardiac rehabilitation (CR) program, especially during summer season.**

Aim: **To assess the effect of Ramadan fasting on biochemical and exercise parameters among patients undergoing 12-week exercise-based CR program.**

Patients and methods: **53 patients joining CR program in university hospital were included in the study. The patients were divided into two groups according to their Ramadan fasting status. Fasting group included 32 patients, while non-fasting group included 21 patients. All patients underwent supervised exercise-based CR during the month of Ramadan. Plasma osmolality, blood urea and serum creatinine were assessed before CR and during the last week of Ramadan. Lipid profile, echocardiography and exercise parameters were assessed before and after CR program.**

Results: **The two groups were similar in baseline characteristics including: risk factors, osmolality, urea, creatinine, lipid profile and hemoglobin values, as well as ejection fraction and exercise parameters. After the program, both groups showed significant improvement in ejection fraction, total cholesterol, LDL and HDL levels. There was also improvement in duration of exercise reached and achieved METs before and after CR program in both groups. An important notice was that fasting did not significantly influence plasma osmolality in either group.**

Conclusion: **Ramadan fasting did not change serum osmolality or negatively affect the results of CR among cardiac patients. It appears to be safe to undergo exercise-based CR during Ramadan even in summer season.**

Keywords: Cardiac Rehabilitation, Ramadan, Fasting, Osmolality, Exercise

1. Introduction

Ramadan fasting, one of the five fundamental rituals of Islam, is practiced by more than 1.5 billion Muslims worldwide. During the month of Ramadan, the ninth lunar month of the Islamic calendar, Muslims are obliged to refrain from eating, drinking, smoking and conjugal relationships from dawn till sunset, which may approach 15-18 hours, especially during summer. This brings about an alteration in the dietary patterns besides the schedule of medication administration which may be influential on cardiac patients [1].

It is not infrequent for many cardiac patients to fast during Ramadan. Though no clear scientific consensus does exist as regards the influence of Ramadan fasting on cardiac patients, a review of Medline literature published by Salim et al. revealed that Ramadan fasting is not associated with any significant clinical deterioration in stable cardiac patients. In a nonrandomized prospective study conducted by Mousavi et al on 148 patients with documented coronary artery disease (but with left ventricular ejection fraction $\geq$ 50%) revealed no

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significant difference, as regards combined endpoint of chest pain and dyspnea, between fasting and non-fasting patients [2].

Cardiac rehabilitation is an important component in the continuum of care for individuals with cardiovascular disease, providing a multidisciplinary education and exercise program to improve morbidity and mortality risk and is endorsed by numerous international societies [3]. However, maintaining supervised exercise-based cardiac rehabilitation whilst fasting during the month of Ramadan, especially during the summer season, might have biochemical and clinical implications that can negatively impact the expected benefits derived from cardiac rehabilitation programs. The aim of this study was to assess the impact of Ramadan fasting on cardiac rehabilitation outcomes in cardiac patients and to evaluate the effects of fasting on their biochemical profiles. To our knowledge, this is the first study evaluating the effects of Ramadan fasting on cardiac patients undergoing supervised exercise-based cardiac rehabilitation.

2. Methods

To study the influence of Ramadan fasting on cardiac patients undergoing cardiac rehabilitation, a total of fifty-three patients at our university hospital cardiac prevention and rehabilitation unit were included in the study. 79.2% of the included participants (42 patients) were referred after sustaining a recent myocardial infarction: 34 patients with ST-elevation myocardial infarction (STEMI) and 8 patients with non ST-elevation Myocardial infarction (NSTEMI), whereas the remaining 20.8% (11 patients) were referred due to symptomatic heart failure.

The study was approved by the department ethical committee. The patients signed an informed consent after attending an educational session that demonstrated the impact of Ramadan fasting on cardiac patients, the feasibility of exercise during fasting and the importance of cardiac rehabilitation for eligible cardiac patients.

Patients were recruited in the study during the couple of weeks prior to the onset of month of Ramadan. Detailed clinical and biochemical assessments as well as a symptom-limited graded exercise stress test (GXT) and echocardiography were performed prior to the onset and after the termination of a 12-week exercise-based cardiac rehabilitation program. Patients with recent acute coronary syndrome (less than a couple of weeks prior to onset of CR), renal impairment (defined as serum creatinine>1.3 g/dl), uncontrolled diabetes mellites, severely impaired LV systolic function (left ventricular ejection fraction<20%) or inability to exercise were excluded from the study.

Abbreviations:

BHR	Basal heart rate
CR	Cardiac rehabilitation
GXT	Graded exercise stress test
HDL:	High density lipoproteins
HRR	Heart rate reserve
LDL:	Low density lipoproteins
LV	Left ventricle
LVEF	Left ventricular ejection fraction
MET	Metabolic equivalent of task
NSTEMI	Non ST-elevation myocardial infarction
PHR	Peak heart rate
RPE	Rating of perceived exertion
SPSS	Statistical Package for Social Sciences
STEMI	ST-elevation myocardial infarction
TC	Total cholesterol (TC)
TG	Triglycerides
THR	Target heart rate

2.1. Laboratory biochemical investigations

Lipid profile (including total cholesterol (TC), triglycerides (TG), low density lipoprotein (LDL), high density lipoprotein (HDL)) was measured after an overnight 12- hour fasting during the week prior to the onset of month of Ramadan (before starting the CR program) and was repeated after the completion of CR program.

LDL-cholesterol was indirectly measured using the Friedewald equation:[4]

$$\text{Calculated LDL (mg/dl)} = \text{TC} - \text{HDL-} (\text{TG}/5)$$

Plasma osmolality was measured during the week prior to the onset of month of Ramadan (before the onset of CR program) and repeated during the last week of Ramadan (in fasting state in the fasting group and non-fasting state in the non-fasting group).

Plasma osmolality was calculated using the validated Worthley et al. equation:[5]

$$\text{Calculated plasma osmolality} = (2 \times \text{serum [Na, in mmol/L]}) + [\text{glucose, in mg/dL}]/18 + [\text{blood urea nitrogen, in mg/dL}]/2.8$$

2.2. Echocardiography

Resting echocardiographic images were acquired in accordance with American Society of Echocardiography guidelines by a cardiac sonographer,

blinded to group allocation [6]. A commercially available ultrasound system (Vivid S5 or E90, GE Medical Systems, Horten, Norway) equipped with a 2.5-MHz multifrequency phased array transducer was used to obtain and analyze images for left ventricular volumes and hence two-dimensional derived left ventricular ejection fraction calculated using the modified Simpson's biplane method from apical two and apical four-chamber images.

2.3. Graded exercise test (GXT)

A symptom-limited graded treadmill exercise test (GXT) was carried out prior to the exercise rehabilitation program to tailor the exercise training program using modified Bruce protocol [7]. The following exercise parameters were assessed: a) Exercise duration, b) estimated achieved metabolic equivalent of task (METs), c) basal heart rate (BHR) and peak heart rate (PHR). The exercise test was repeated after completion of the 3-month CR program to assess the change in functional capacity of the patients with respect to the aforementioned parameters.

2.4. Exercise rehabilitation program

Fifty-three participants attended the cardiac rehabilitation (CR) program at our university hospital CR unit biweekly in 30-40-minute sessions through 12 weeks with an adherence rate of 85% (20 of 24 sessions) designated as the required standard for inclusion. Beside offering supervised exercise training biweekly, the program also included nutrition and smoking cessation advice serving the purpose of guiding patients towards a healthy lifestyle and reinforcing the practice of moderate exercise outside the hospital. Endocrinology and psychiatry consultations were available as needed.

During the exercise sessions, patients were meticulously monitored and were supervised by a physician. Each session was organized in the following phases: 5–10 minute of treadmill warm up, followed by 20-30 minutes of aerobic continuous treadmill training and terminated by 5-10 minute of cooling down exercises [7]. The exercise intensity was based on the heart rate reserve (HRR), and the target Heart rate (THR) calculated according to the Karvonen method [8] (from the GXT) and complemented by the subjective rating of perceived exertion (RPE) measured by Borg's scale [9]. Patients included in this group were subjected to moderate intensity exercise training with gradually increasing intensity of exercise level grading from 40% to 60% of HRR [10].

THR = rest heart rate +40%-60% of HRR, where HRR was calculated as (HRR = peak heart rate − basal heart rate).

Exercise intensity and training heart rate range were re-prescribed every two weeks based on RPE keeping it between 11-13 on Borg scale. The duration of exercise was progressively increased from 20 to 30 minutes by the fifth week and was maintained thereafter. Whilst further non-structured, home-based exercise was advised in line with guidelines for secondary prevention, this aspect of the program was not monitored or quantified [11].

The patients were divided into two groups according to their Ramadan fasting status. Fasting group included 32 patients, while non-fasting group included 21 patients. All patients underwent exercise training during cardiac rehabilitation in Ramadan. Blood tests, echocardiography and exercise parameters were assessed before and after cardiac rehabilitation program.

Only the patients who completed the 3 month CR program in our unit attending >85% of the exercise training sessions (20 of 24 sessions) including at least 6 out of 8 of the sessions during the month of Ramadan were included in the study.

3. Statistical methods

Statistical analysis was done using the Statistical Package for Social Sciences (SPSS) version 22.0 for Windows (IBM© Corp., Armonk, NY, USA). Numerical data were expressed as mean and standard deviation. Qualitative data were expressed as frequency and percentage. Chi-square test or Fisher's exact test was used to examine the relation between qualitative variables. For quantitative data, comparison between two groups was done using either Student t-test for normally distributed data or Mann-Whitney test (non-parametric t-test) for not normally distributed data. Paired t-test or Wilcoxon-signed ranks test (non-parametric paired t-test) was used to compare two consecutive measures of numerical variables. All tests were two-tailed. A p-value < 0.05 was considered significant.

4. Results

Both groups were similar in baseline demographic characteristics including age and gender as well as cardiovascular disease risk factors (Table 1). All prescribed cardiovascular medications remained unchanged during the study period. No cardiovascular complications or other adverse events were experienced by the participants in either group. There was no statistically

Table 1. Baseline demographic, clinical, biochemical, echocardiographic and exercise parameters.

Variables	All patients	Fasting group	Non-fasting group	P-value
Number of patients	53	32 (60.4%)	21 (39.6%)	
(I) Demographics				
Age (years)	51.4 ± 10.2	50.28 ± 9.95	53.0 ± 10.68	0.357
Gender				
Males	45 (84.9%)	26 (81.3%)	19 (90.5%)	0.455
Females	8 (15.1%)	6 (18.8%)	2 (9.5%)	
(II) Risk factors				
Hypertension	17 (32.1%)	9 (28.1%)	8 (38.1%)	0.447
Diabetes mellites	19 (35.8%)	10 (31.3%)	9 (43%)	0.604
Current smoking	22 (41.5%)	14 (43.8%)	8 (38.1%)	0.064
Etiology				
Ischemic	42 (79.2%)	23 (71.9%)	19 (90.5%)	0.102
Non-ischemic	11 (20.8%)	9 (28.1%)	2 (9.5%)	
(III) Laboratory biochemical parameters				
Osmolality (mOsm/kg)	276.82 ± 14.02	277.91 ± 15.14	279.46 ± 8.63	0.640
Blood urea (mg/dl)	30.66 ± 10.83	31.3 ± 10.3	29.6 ± 11.8	0.536
Serum creatinine (mg/dl)	1.04 ± 0.23	1.01 ± 0.24	1.10 ± 0.22	0.122
Fasting blood sugar (mg/dl)	141.38 ± 66.86	137.9 ± 63.0	146.7 ± 73.6	0.630
Total cholesterol (mg/dl)	174.04 ± 41.41	174.8 ± 40.8	172.9 ± 43.3	0.920
Triglyceride (mg/dl)	155.06 ± 63.38	162.3 ± 65.4	144.0 ± 60.0	0.220
HDL-cholesterol (mg/dl)	41.87 ± 9.62	42.7 ± 10.6	40.6 ± 8.0	0.397
LDL-cholesterol (mg/dl)	102.19 ± 36.77	100.7 ± 33.4	104.5 ± 42.1	0.785
(IV) Echocardiography				
LVEF%	45.4 ± 13.8	48.2 ± 13.2	41.1 ± 13.8	0.052
(V) Exercise parameters				
METs	8.98 ± 2.84	9.2 ± 2.8	8.7 ± 2.9	0.501
Duration (minutes)	11.79 ± 3.64	12.2 ± 3.4	11.2 ± 3.9	0.467
BHR (bpm)	75.81 ± 11.48	76.2 ± 11.0	75.3 ± 12.5	0.722
PHR (bpm)	130.57 ± 18.92	131.4 ± 19.2	129.3 ± 18.9	0.616

Abbreviations: LVEF, left ventricular ejection fraction; MET, metabolic equivalent of the task; BHR, basal heart rate; PHR, peak heart rate; mg/dl, milligram per deciliter; p-value is calculated for the fasting and non-fasting groups.

significant difference between both groups as regards all baseline laboratory biochemical parameters (osmolality, blood urea, serum creatinine, fasting blood sugar and lipid profile), left ventricular ejection fraction and all baseline exercise parameters (METs, duration, BHR and PHR), as shown in table (1).

4.1. Laboratory biochemical parameters

Both groups showed no significant difference between the baseline and follow-up values of serum creatinine, blood urea, osmolality and blood sugar, with no significant percent change between both groups (Tables 2 and 3, Fig. 1).

After CR program completion, although both groups showed a favorable change in cholesterol levels (showing a significant decline in total cholesterol and LDL-cholesterol with concomitant significant elevation in HDL-cholesterol), no significant effect of fasting on the percent change in the aforementioned cholesterol parameters. Regarding triglycerides, although there was a significant decline in the fasting group, in contrary to the non-fasting group, there was no significant difference between both groups as regards the percent change in triglycerides (Table 3).

4.2. Echocardiography

As shown in Table 3, fasting did not negatively influence the beneficial effect of CR on LVEF. Owing to undergoing CR, both groups exhibited a statistically significant improvement in LVEF, nevertheless, with a similar magnitude of improvement ($p > 0.05$).

4.3. Exercise parameters

Ramadan fasting did not significantly attenuate the favorable effects of CR on exercise parameters. Both groups showed a significant improvement in post-CR exercise test parameters as regards METs and exercise duration compared to pre-CR exercise test, albeit at a similar magnitude ($p > 0.05$ as regards percent change between both groups). In addition, no significant difference between both groups as regards the percent change in BHR and PHR.

Table 2. Percent change from baseline in both groups regarding biochemical and exercise parameters as well as LVEF.

	Fasting group (percent change from baseline)	Non-fasting group (percent change from baseline)	P- value (Mann-Whitney test)
(I)Laboratory biochemical parameters			
Osmolality	1.4 ± 6.86	1.7 ± 4.56	0.850
Blood urea	−2.59 ± 33.93	7.07 ± 45.33	0.513
Serum creatinine	−5.47 ± 19.24	−4.53 ± 22.20	0.689
Fasting blood sugar	5.2 ± 32.36	5.2 ± 36.70	0.813
Total cholesterol	−1.97 ± 13.79	−5.03 ± 9.82	0.827
Triglyceride	−1.97 ± 19.34	−3.35 ± 18.59	0.884
HDL-cholesterol	4.99 ± 11.14	11.36 ± 13.49	0.131
LDL-cholesterol	−2.52 ± 18.80	−6.98 ± 15.89	0.467
(II) Echocardiography			
LVEF%	9.60 ± 13.47	18.18 ± 20.41	0.111
(III) Exercise parameters			
METs	27.32 ± 33.18	34.49 ± 73.63	0.688
Duration	22.01 ± 45.32	25.90 ± 40.42	0.746
BHR	−5.90 ± 13.18	−1.02 ± 20.23	0.156
PHR	1.33 ± 15.72	1.15 ± 16.56	0.569

Table 3. Biochemical, echocardiographic and exercise parameters in fasting and non-fasting groups at baseline and at follow-up.

	Fasting group (n = 32)			Non-fasting group (n = 21)		
	Before CR	After CR	P-value	Before CR	After CR	P-value
(I) Laboratory biochemical						
Osmolality (mosm/kg)[a]	277.91 ± 15.14	281.01 ± 11.61	0.341	279.46 ± 8.63	283.88 ± 6.68	0.071
Blood urea (mg/dl)[a]	31.3 ± 10.3	29.3 ± 11.9	0.489	29.6 ± 11.8	29.1 ± 12.8	0.837
Serum creatinine (mg/dl)[a]	1.01 ± 0.24	0.93 ± 0.22	0.107	1.1 ± 0.22	1.03 ± 0.24	0.149
Fasting blood sugar (mg/dl)[a]	137.9 ± 63	140.3 ± 76.5	0.694	146.7 ± 73.6	143 ± 67.2	0.779
Total cholesterol (mg/dl)	174.8 ± 40.8	169.4 ± 37.1	0.034	172.9 ± 43.3	163 ± 40.7	0.011
Triglyceride (mg/dl)	162.3 ± 65.4	152.8 ± 52.3	0.042	144 ± 60	133.9 ± 48.4	0.149
HDL-cholesterol (mg/dl)	42.7 ± 10.6	44.5 ± 10.9	0.029	40.6 ± 8	45 ± 8.9	<0.001
LDL-cholesterol (mg/dl)	100.7 ± 33.4	94.5 ± 26.1	0.023	104.5 ± 42.1	93.8 ± 33.8	0.005
(II) Echocardiography						
LVEF	48.2 ± 13.2	52 ± 12.8	<0.001	41.1 ± 13.8	47.6 ± 14.5	0.002
(III) Exercise parameters						
METs	9.2 ± 2.8	11.2 ± 3.1	<0.001	8.7 ± 2.9	10.6 ± 3.1	0.002
Duration (min)	12.2 ± 3.4	13.99 ± 3.3	<0.001	11.2 ± 3.9	13.32 ± 3.93	0.002
BHR (bpm)	76.2 ± 11	71 ± 10.6	0.007	75.3 ± 12.5	73.1 ± 14.4	0.732
PHR (bpm)	131.4 ± 19.2	131.3 ± 17.7	0.460	129.3 ± 18.9	129.2 ± 19.3	0.958

[a] Parameters assessed at baseline and during the last week of Ramadan (in fasting state in the fasting group and non-fasting state in the non-fasting group).

5. Discussion

To our knowledge, this is the first study to address both safety and efficacy of undergoing supervised exercise-based 12-week CR as secondary prevention for acute coronary syndrome or symptomatic heart failure whilst Ramadan fasting and to study whether Ramadan fasting negatively influences the beneficial effects of CR or not.

CR is currently a class I indication in most clinical practice guidelines, including those with acute coronary syndromes and heart failure [12–14]. The beneficial effects of CR has been further re-emphasized in a Cochrane systematic review and meta-analysis conducted by Anderson et al. in 2016 that confirmed that exercise-based CR reduces cardiovascular mortality and hospital admissions and improves quality of life [15].

In our cohort, CR did improve functional capacity, objectively assessed by exercise parameters (exercise duration and achieved METs) in both fasting and non-fasting groups. This is consistent with Mohammadifard et al. who investigated patients with mild to moderate left ventricular dysfunction who participated in an 8-week exercise-based CR, where post CR, peak exercise capacity increased from 8.00 ± 2.56 to 10.08 ± 3.00 METs ($p < .001$) and exercise duration increased from 14.17 ± 5.27 to 17.21 ± 5.85 minutes ($p < .001$) [16].

Regarding lipid profile, our study showed a favorable effect of CR on total cholesterol, LDL and HDL whether fasting or not. This is also consistent

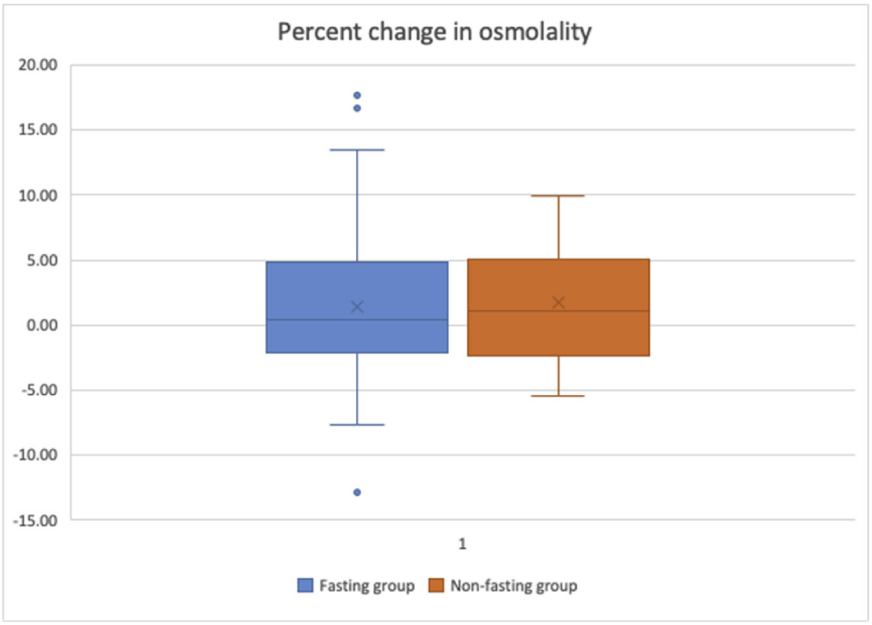

Fig. 1. Percent change osmolality in fasting and non-fasting groups.

with Mohammadifard et al. who showed that an 8-week CR program significantly reduced total cholesterol and LDL-cholesterol, with concomitant significant increase in HDL-cholesterol [16].

With respect to the effect of CR on LV systolic function, our findings showed a significant improvement in LVEF in both groups ($p < 0.05$). Other Studies investigating the effect of CR on LV systolic function have yielded conflicting results. After acute myocardial infarction, Jiang et al. showed that CR significantly improved LVEF [17], unlike what was concluded by McGregor et al. [18]. Also, in patients with heart failure with reduced ejection fraction, a meta-analysis of exercise training on LVEF showed that moderate-intensity continuous training significantly increased LVEF (95% confidence interval, CI, 2.08 to 5.50%) [19]. On the contrary, McKelvie et al. showed no significant impact [20]. As most of the study population in our study were post myocardial infarction patients that were revascularized, the significant improvement in LVEF after 3 months may be partially attributed to the process of reverse remodeling that is accelerated by guideline directed pharmacotherapy and revascularization in addition to the favorable effects of exercise-based cardiac rehabilitation.

The current study demonstrated no negative influence of fasting on cardiac patients undergoing supervised exercise-based cardiac rehabilitation. This result is concordant with **Güvenç A** study result who investigated this effect on young soccer players and concluded that if regular training regimen, body fluid balance, daily energy intake and sleep duration are maintained as before Ramadan, Ramadan fasting does not have detrimental effects on aerobic exercise performance or body composition in young soccer players [21].

In our study, renal functions were not altered due to Ramadan fasting, which is consistent with Asegaonkar S et al who achieved the same results among healthy individuals [22]. Besides, no attenuation of the favorable effects of CR on lipid profile parameters occurred due to Ramadan fasting. It is worth mentioning that effect of Ramadan fasting on blood lipids yielded inconsistent and even conflicting findings among various studies, which was attributed to the amount and type of food intake, physical activity, ethnic, and genetic background of studied populations [23,24].

It has been intriguing to study the effect of Ramadan fasting on plasma osmolality in patients undergoing exercise-based CR. Plasma osmolality, which is the sign of osmotic activity of all plasma solutes, is between 275-295 milliosmol in one kilogram (mosm/kg) in mature people. It is primarily determined by serum electrolytes (mainly sodium), glucose and urea. Various conditions are associated with increased (hyperglycemia, diabetic ketoacidosis, diabetes insipidus, nonketotic hyperosmolar hyperglycemic coma, dehydration, hypernatremia, alcohol ingestion) and decreased (hyponatremia, syndrome of inappropriate antidiuretic hormone, nephrotic syndrome, adrenal insufficiency, liver cirrhosis, congestive heart failure) serum osmolality.

In our current research, no significant difference was detected between the fasting and non-fasting status with no significant change in either group regarding plasma osmolality. This can be explained by osmoregulation that is mainly controlled by osmoreceptors (located mainly in the hypothalamus). It occurs by negative feedback: when plasma osmolality increases, due to water deprivation, for instance, osmoreceptors are stimulated which leads to stimulation of thirst and antidiuretic hormone secretion that subsequently decreases plasma osmolality by enhancing water reabsorption via the late distal convoluted tubule and collecting ducts. The opposite happens when plasma osmolality decreases [5,25]. Our findings do commensurate with those concluded with Dikme et al who showed no effect of Ramadan fasting on serum osmolality in emergency patients [26] and Attarzadeh et al who also demonstrated no effect of Ramadan fasting and physical activity in females on serum osmolality [27]. Besides, in a study by Ziaee et al, despite occurrence of increased osmolality during Ramadan fasting, the measurements remained within normal range [25].

6. Conclusion

Our study demonstrated both safety and efficacy of undergoing supervised exercise-based cardiac rehabilitation whilst Ramadan fasting, even during the summer season. Ramadan fasting did not attenuate the beneficial effects of CR on functional capacity, LVEF and lipid profile. It did not also alter either renal function or plasma osmolality.

7. Study Limitations

Limitations of the current study warrant discussion. Firstly, due to ethical constraints, participants were not randomly assigned. Although this lack of randomization cannot be excluded as a confounding variable, its influence on the results is likely to be minimal as the groups were well matched for all baseline demographic, clinical, laboratory, echocardiographic and exercise test variables. Secondly, our sample size was relatively small and thirdly the majority of the participants were males. Future large-scale multi-center studies are required to confirm these results.

Author contribution

Hazem Khorshid, Adel Shabana, Osama Rifaie, Yasser Abdellatif: CONCEPTION Constructing an idea or hypothesis for research and/or manuscript, **DESIGN** Planning methodology to reach the conclusion, **FUNDINGS** Providing personnel, environmental and financial support and tools and instruments that are vital for the project.

Hazem Khorshid, Osama Rifaie: SUPERVISION Organising and supervising the course of the project or the article and taking the responsibility.

Hazem Khorshid, Adel Shabana: MATERIALS Biological materials, reagents and referred patients, **DATA COLLECTION AND/OR PROCESSING** Taking responsibility in execution of the experiments, patient follow-up, data management and reporting.

Hazem Khorshid, Osama Rifaie, Yasser Abdellatif: ANALYSIS AND/OR INTERPRETATION Taking responsibility in logical interpretation and presentation of the results; **LITERATURE REVIEW** Taking responsibility in this necessary function.

Hazem Khorshid, Yasser Abdellatif: WRITER Taking responsibility in the construction of the whole or part of the manuscript, **CRITICAL REVIEW** Reviewing the article before submission not only for spelling and grammar but also for its intellectual content.

Declaration of Competing Interest

The authors declare that there is no conflict of interest.

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