Original Article

To Show the Effect of Intermittent Fasting during Ramadan on Endothelial Dysfunction via TIMI Frame Count

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Abstract

Background: Fasting and coronary functions are prestige fields for the study. There are a limited number of studies on these topics. The effect of Ramadan fasting on endothelial dysfunction, which can be manifested by loss of nitric oxide bioavailability, has been demonstrated via flow-mediated vasomotion in patients with the slow coronary flow in a small number of studies. To our knowledge, there is no study showing the relationship between TIMI frame count and Ramadan fasting. **Aims:** We aimed to prove that Ramadan fasting can improve endothelial dysfunction which can be documented via the TIMI frame count method in angiography. **Method:** This retrospective study included 67 patients diagnosed with the coronary slow flow by coronary angiographic before Ramadan. All of them were evaluated again via TIMI frame count within a period of 1 to 3 months after Ramadan. We tested our hypothesis that fasting may improve endothelial dysfunction and it was proved by the TIMI frame count method in our study. **Results:** TIMI frame counts measured angiographically from LAD, Cx, and RCA and they were significantly lower than the counts before fasting. All coronary frame count parameters showed significant improvement after Ramadan compared with the baseline values before the Ramadan fasting period ($P < 0.001$). **Conclusion:** Our results revealed that fasting and lifestyle changes during Ramadan may be beneficial for the improvement of endothelial dysfunctions in patients with the slow coronary flow and this can be showed easily using TIMI frame count. This is a practical and easy method for showing coronary functions.

Keywords: *Coronary artery disease, coronary slow flow, fasting, Ramadan, TIMI frame count*

Background

Slow coronary flow (SCF) is frequently encountered during coronary angiography and is characterized by delayed opacification of the distal vascular bed in the presence of normal or minimal arteriosclerotic coronary arteries in angiography. Tambe *et al*.[1] were the first to describe this phenomenon in patients without an atherosclerotic lesion. Recently, capillary disorders were found responsible for decreased coronary flow.[2] Microvascular dysfunction is associated with endothelial and vasomotor dysfunction while occlusive coronary artery disease and myocardial ischemia are associated with the impaired coronary flow.[3-7] In the view of these data, SCF can be described as an early stage of atherosclerosis in small coronary arteries.

Almost one billion Muslims experience fasting along with lifestyle changes during Ramadan in the world. However, there is an inadequate number of studies on the effects of fasting on endothelial functions during Ramadan which may be manifested by a decrease in nitric oxide levels as demonstrated in patients with SCF.[1,2]

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During the period of Ramadan, healthy Muslims avoid eating, drinking, sexual relationships, and smoking from dawn to dusk. Ramadan follows the lunar calendar and hence the fasting month comes earlier about 10 days every year. This brings about a change of the season of fasting month in addition to the length of the fasting time which may vary from 11 to 18 h. During Ramadan fasting, Muslims eat two meals a day, one before dawn (Suhoor meal) and the other shortly after sunset (Iftar meal). These changes in dietary patterns and meal schedules are associated with changes in sleeping habits.[8] This lifestyle change in terms of taking daily calorie intake via two meals with alteration of medication schedule might affect patients with cardiovascular diseases (CVD).[9] Muslims with risk for health are exempted from fasting. The Qur'an states that fasting during illness must be avoided.

Nematy *et al*.[10] have demonstrated a significant improvement in 10-year risk factors based on Framingham risk score after Ramadan fasting. There were significantly higher levels of high-density lipoprotein cholesterol (HDL-C), lower low-density lipoprotein cholesterol (LDL-C), body mass index, and waist circumference after Ramadan. All these factors could be beneficial for the cardiovascular system.

Endothelial dysfunction during Ramadan, which can be detected by loss of nitric oxide bioavailability, is an increasingly encountered cause of CVD. The studies showed that diet affects endothelial function and may modify cardiovascular risk. In a small study of 21 male patients with cardiovascular risks, Yousefi *et al*.[11] reported that nitric oxide levels were significantly higher after Ramadan fasting compared with the baseline value.[11-13]

There is no study about the comparison of endothelial functions via angiographically before and after Ramadan. We aimed to prove that fasting and lifestyle changes during Ramadan can improve endothelial functions in patients with the SCF and it can be evaluated with thrombolysis in myocardial infarction (TIMI) frame count (TFC) in coronary angiography.

Materials and Methods

Study design and patients

This retrospective study was performed at the Bicard clinic in Bishkek/in Kirghizstan during the Ramadan period which started in May 2017 and finished in June 2017. The present study included 67 consecutive patients with SCF. They all had undergone coronary angiography within a period of 1 to 3 months before Ramadan and diagnosed with the coronary slow flow for all coronary arteries. All of them underwent coronary angiography after Ramadan within a period of 1 to 3 months in the same institutions for different reasons again. Also, they were on the same medications (angiotensin-converting enzyme [ACE] inhibitors, acetylsalicylic acid, Ca-channel blockers, β–blockers) the exclusion criteria were occlusive ischemic heart disease, renal failure, noncardiac fluid overload, thyroid disorders, or liver diseases, diabetes, and different medications.

The cineangiography records of 67 consecutive patients were examined for SCF via TFC measurements. Their coronary angiograms were performed via the femoral approach using the standard technique and iopromide for contrast enhancement (cineangiographic equipment: Philips Integris H 3000, Holland; cine frame: 30 fps). We measured the number of cine frames required for the contrast to first reach standard distal coronary landmarks for each coronary arteries. The first frame is defined as the one where the column of nearly or fully concentrated dye is seen extending across at least 70% of the arterial lumen with antegrade dye motion, and the last frame counted is that in which contrast first appears in the distal predefined landmark branch, but full opacification of the branch is not necessary.[12] The distal coronary landmarks used for analysis were the distal bifurcation at the apex of the left anterior descending coronary artery (LAD) (the mustache, pitchfork, or whale's tail), the distal bifurcation of the major obtuse marginal or the main circumflex coronary artery (Cx), whichever was larger, and the site of origin of the first branch at the crux or its poster lateral extension for right coronary artery (RCA). The cine film was run past the initial opacification of the end branch and then was moved frame by frame in reverse until the end branch disappeared before catching the last frame. Then the frame count for each artery was done by subtracting the first frame from the last frame. The frame count was corrected by dividing with 1.7 to derive a corrected TFC. The diagnosis of the SFC can be made based on the TIMI flow grade or TFC. TIMI-2 flow grade (i.e. requiring ≥ 3 beats to opacify the vessel) or a corrected TFC > 27 frames has been frequently used.[12] After that, all TFC results had been evaluated and compared statistically.

Statistical analysis

The statistical package for the social sciences, version 17.0, (SSPS Inc, Chicago, Ill, USA) was used for statistical analysis. Continuous variables were expressed as means ± standard deviation. Categorical variables were expressed as the total number (percentage). The analysis was performed using the Student's *t*-test. Categorical

data were compared against a Chi-square distribution. A P value < 0.05 was regarded as significant.

Results

The baseline characteristics of the patients were shown in Table 1 and there was no statistically significant difference in biochemical and other parameters before and after Ramadan [Table 1]. Corrected TFC for each artery and mean TFC are shown in Table 2. And there were statistically significant differences before and after Ramadan. (P < 0.001)

Corrected frame counts before Ramadan in patients with SCF were (mean TFC: 30 ± 7, LAD: 31 ± 10, Cx: 27 ± 8 and RCA: 33 ± 9 frames/s), respectively. After Ramadan, all TFC parameters decreased (Mean TFC: 16 ± 3, LAD: 16 ± 4, Cx: 17 ± 3, and RCA: 15 ± 4 frames/s), P < 0.001, respectively.

Discussion

Ramadan fasting, as the main ritual of Islam, is fasting during the holy month of Ramadan. In this month, Muslims, which are more than one billion, change their eating and drinking habits from dawn to sunset. A radical change in lifestyle during Ramadan has a significant impact on the heart and vascular bed.[13,14] Qur'an, the holy book of Islam, support moderate eating, physical exercise, engaging in spiritual activities, and abstention from forbidden foods and drinks.[15] In other words, the Ramadan period includes not only fasting but also radical changes in lifestyle and moral values.[15,16] Weight loss, cessation of smoking occurs during Ramadan fasting. These changes, especially are beneficial in patients with cardiovascular disease, metabolic syndrome, type 2 diabetes, and obesity.[15,16]

In our study, we have attempted to demonstrate the effect of Ramadan on endothelial dysfunction via the TFC method. Consequently, we evaluated the changes in 67 patients in terms of TFC before and after Ramadan retrospectively.

It has been reported that there was an improvement in some biochemical values after Ramadan fasting. There was a significant increase in HDL-C and a decrease in low-density LDL-C after Ramadan.[11,15,16]

The same changes in lipid profile, blood pressure, body mass index was not observed in our study after Ramadan. This discrepancy can be due to our study duration which is shorter than other studies. But still, we observed improvement of endothelial dysfunction.

Some studies are revealing dietary approaches improving endothelial oxidative stress and dysfunction. Reduced calorie intake, which lessens oxidative stress formation in the mitochondria, and, as a result of this, reducing oxidative damage to the cells, may play a role in improving endothelial dysfunction.[17-19] However, to our knowledge no study with TFC evaluating endothelial function before and after Ramadan has been found in the literature.

Endothelial dysfunction stems from nitric oxide synthesis reduction and it is a marker of the early stage of arteriosclerotic disease. Studies are demonstrating dietary effects on endothelial function. In a small study of 21 male patients with cardiovascular risks, Yousef *et al*.[11] reported that nitric oxide levels were significantly higher after Ramadan fasting compared with the baseline value.

Although most studies have reported significant weight loss during Ramadan, almost all of them reported a uniform weight to regain after Ramadan as well in a meta-analysis by Sadeghirad *et al*.[16] Although all body mass indexes (BMIs) and clinical parameters were the same before and after Ramadan in our study, alternation of lifestyle and eating habits can play a role

Table 1: The characteristics of the study population (n = 67)

	Before Fasting	After Fasting	P-value
Age, years	68 ± 5.4	68 ± 5.4	-
Sex, male, n (%)	34 (51)	34 (51)	-
Smoking, n (%)	32 (48)	35 (53)	P = 0.85
Mean LVEF, %	62 ± 5	63 ± 6.6	P = 0.98
Mean blood pressure (mmHg)	103 ± 20	102 ± 24	P = 0.69
Mean blood pressure (mmHg)	103 ± 20	102 ± 24	P = 0.69
Heart rate (beats/min)	77 ± 16	76 ± 14	P = 0.65
LDL cholesterol (mg/dL)	110 ± 24.7	108 ± 26.8	P = 0.71
HDL cholesterol (mg/dL)	38 ± 9.4	38 ± 8.0	P = 0.89
Body mass index (kg/m^2)	28.6 ± 3.9	28.2 ± 4.8	P = 0.78
Creatinine, (mg/dL)	0.8 ± 0.19	0.78 ± 0.16	P = 0.61
Hemoglobin, (g/dL)	13 ± 1.4	13 ± 1.4	P = 0.25
Fasting blood glucose (mg/dL)	104 ± 39	103 ± 38	P = 0.33
BUN, mg/dL	12 ± 0.9	11 ± 0.7	P = 0.57

Table 2: Corrected TFC for each coronary artery and mean TFC before and after Ramadan fasting

	Before Fasting	After Fasting	P-value <
CTFC-LAD, frames/s	31 ± 10	16 ± 4	0.001
CTFC-RCA, frames/s	33 ± 9	15 ± 4	0.001
CTFC-Cx, frames/s	27 ± 8	17 ± 3	0.001
Mean TFC, frames/s	30 ± 7	16 ± 3	0.001

in improving endothelial function via different ways like insulin resistance and other metabolic alternations. It has been shown that fasting can improve blood insulin levels. Besides, the American Diabetic Association advised that fasting can be a modality of type II diabetes treatment and it is documented that insulin is a potent vasoconstrictor molecule. A decrease in insulin levels can improve endothelial dysfunction.[20-23] Furthermore, it should be taken into consideration that our study population abstained from alcohol intake and smoking cigarettes during the fasting period as a part of their religion and more active due to Islamic rituals like performing salaat. Our results also show that fasting and lifestyle changes during Ramadan may be beneficial to improve endothelial dysfunctions in patients with SCF and this can be shown easily using TFC. Lifestyle changes cannot be homogenized in our study but fasting and fasting periods were homogeneous owing to Islamic rules. Also, intermittent fasting has a lot of fruitful effects such as improving the immune system and reducing inflammation.[18,24-26]

Our study had some shortcomings. Our study population was small and evaluated retrospectively. They could not be observed for a long period. But our study only tested the effects of fasting on coronary endothelium invasively via TFC. We did not evaluate the monocular basis of fasting. Intermittent fasting is getting popularity for the treatment of some metabolic conditions. Our study showed the relation of improving SCF and fasting via angiographically.

Conclusion

We showed via coronary angiography and TFC that fasting during Ramadan in patients with coronary slow flows improves endothelial dysfunction and intermittent fasting can be used as a treatment option in coronary slow flow patients. Also, there is a need for large-scale studies and an explanation of the monocular basis of fasting on endothelial dysfunction during Ramadan.

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Conflicts of interest

There are no conflicts of interest.

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