



The Impact of Diurnal Fasting During Ramadan on Patients with Established Cardiac Disease: A Systematic Review

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Abstract

During the month of Ramadan, Muslims abstain from eating before dawn until after sunset for a month. This study reviews most recent literature on the effect of Ramadan fasting on the Cardiac patient specifically, excluding any study done on patients with no diagnosis of Cardiac disease to help cardiologists better deal with their patients who would wish to fast during Ramadan. As such, a Medline and Pubmed search was conducted to retrieve studies investigating the effects of fasting during Ramadan specifically on the cardiac patient with regard to incidence of cardiac disease and change in cardiovascular risk parameters. The search was conducted by combining the key word "Ramadan Fasting" with multiple cardiac diseases and cardiovascular risk parameters. Only studies reporting results on patients already diagnosed with a cardiac disease were included. fourteen were included. Most studies have shown, with a few exceptions, that Ramadan fasting has no adverse effects on incidence of cardiovascular disease or the number of hospitalizations due to cardiac disease events. Thus patients with controlled disease may fast with the consultation and monitoring of their physician.

Keywords: Ramadan Fasting; Cardiac Disease; Cardiovascular Risk Factors.

Citation: Refaat M, El Jamal N, El-Rayess H, Gebran A, Salam A. The Impact of Diurnal Fasting During Ramadan on Patients with Established Cardiac Disease: A Systematic Review: International Cardiovascular Forum Journal. 2018;15:12-18. DOI: 10.17987/icfj.v15i0.549

Introduction

Fasting in the month of Ramadan of the Islamic calendar is one of the pillars of Islam. It is an obligation for all Muslim adults. In Ramadan, Muslims refrain from the consumption of food and fluids from the rising to the setting of the sun, and have two meals; one at the breaking of the fast (Iftar) and one before sunrise (Suhur). On top of its religious significance, recent studies showed several benefits of fasting that promote cellular regeneration, reversing immunosuppression and diabetes. [1, 2] Other recent studies demonstrated a possible benefit of fasting in cancer prevention, ameliorating toxicity and efficacy of chemotherapy,[3-9] preserving cognitive performance,[10] and improving outcome in studies on neurodegenerative diseases. [11, 12]

In light of its religious importance and the benefits fasting might

have, physicians are asked by their patients if it is safe for them to fast. Of particular interest to us is the cardiac patient as many seek the advice of their cardiologist regarding their ability to fast. This review aims to investigate the available evidence-based literature on the effects of Ramadan fasting on the cardiac patient.

Methods

The studies addressed in this review were obtained by a Medline and Pubmed search using the key word "Ramadan fasting" combined with the mesh terms "Coronary Heart Disease", "Heart Failure", "atrial fibrillation", "angina", "myocardial Infarction", "arrhythmia", "cardiovascular disease", "cardiovascular disease AND diabetes", OR "stroke". The search period was set until 31 December 2017. Titles and abstracts were examined

independently by two investigators for relation to our topic. Those related, were in the same way examined according to the following inclusion and exclusion criteria. All articles, letters, and reports describing statistical, experimental, or case studies on the effects of Ramadan fasting on cardiac patients, the incidence of cardiac disease, and cardiovascular risk factors in these patients were included. The criteria for exclusion were reviews, articles not written in English, and studies depicting effect of Ramadan fasting on parameters in previously healthy individuals since our study is concerned with the cardiac patient. Studies that investigated effects of Ramadan fasting on incidence of cardiovascular events or cardiovascular risk factors in all patients, but specified results for previously diagnosed cardiac patients, were included and only data on cardiac patients was extracted. Studies that fit the inclusion criteria were then examined and their results extracted into a database and noted for the presence or absence of any significant difference attributed to Ramadan Fast. Secondary outcomes of studies were also extracted and analysed. Risk of bias and the quality of the studies were assessed by using the NIH Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies.[13]

Results

The search yielded 178 results after removing duplicates. The process of screening the articles is represented in the flow diagram of Figure 1. Of the search, fourteen met our inclusion criteria; i.e. relating fasting to effects on cardiac patients, along with two case studies. Of these nine reported a relation between incidence of cardiovascular disease or hospitalization due to cardiac events and Ramadan fasting (Table 1). These were important to include as they indicated effects of fasting on patients already diagnosed with these conditions or who previously had these conditions. Five studies investigated effects of Ramadan fasting on cardiovascular risk factors in patients diagnosed with cardiac disease, or with previous cardiac disease (Table 2). Most studies included had a good or fair quality rating after quality assessment by the NIH quality assessment tool (Table 3). The search also yielded two case studies. One of which reported polymorphic ventricular tachycardia in a patient with known brugada syndrome after a large meal and a month of fast.[14] The other case study reports a patient with hypertension, hyperlipidemia, and diabetes type 2 who experienced angina while fasting during Ramadan, symptoms were relieved with medical treatment after the fast, but then the patient suffered a new thrombotic occlusion leading to four vessel bypass surgery.[15]

3.1 Effects of Ramadan Fasting on Incidence of Cardiovascular Events in Patients with Heart Disease:

Most studies tabulated in Table 1 showed no significant difference between Ramadan and non-Ramadan months regarding incidence of cardiovascular events (Stroke, Myocardial Infarction, Unstable Angina, Atrial Fibrillation, Heart Failure) in the different categories of cardiac patients.[13, 16-23] However patients with a previous MI were shown to be less likely to be hospitalized for CHF,[16] and for Atrial Fibrillation during Ramadan compared to other months. In a study involving 4175 patients Salam et al. reported that patients admitted for hospitalization due to Heart Failure during Ramadan were more likely to have previous CAD compared to non-Ramadan months.[23] Moussavi et al.[24] and Chamsi Pasha at al.[17] reported no significant effect of Ramadan fasting on chest pain, discomfort, or precipitation of cardiac events.

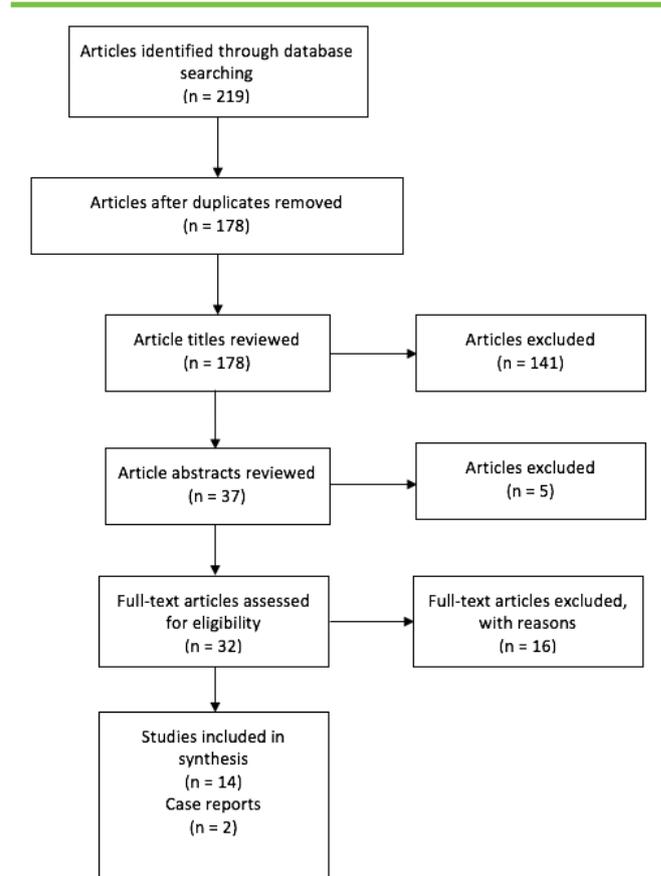


Figure 1. Flow diagram of the selection process.

3.2 Effects of Ramadan Fasting on Lipid Profile in Cardiac Patients:

Effects of Ramadan fasting on HDL are different across the studies tabulated. While Yousefi et al.[25] reported amelioration of HDL levels during Ramadan fast in patients with previous cardiovascular disease, Khafaji et al. reported a significant decrease in HDL levels in stable cardiac patients.[26] Also the study by Khafaji et al. is the only study reporting a significant increase in LDL in fasting, while the rest report either no significant change in LDL levels. [25] All studies that measured total cholesterol in cardiovascular patients reported no significant change in its levels during fasting [19, 25, 26] except Nematy et al. who reported amelioration in lipids profile.[27]

3.3 Effects of Ramadan Fasting on Cardiovascular Risk Factors in Patients with Cardiovascular Disease:

Regarding fasting blood sugar levels, no study showed a significant change during fasting compared to non-fasting months in cardiovascular patients.[25, 27] Inflammatory profiles, and vasculoprotective indicators were reported to either not change significantly,[26, 27] or to ameliorate[25] in Ramadan in patients with cardiovascular disease. Nematy et al. also reported an improvement in 10 year coronary heart disease risk in patients with cardiovascular disease during Ramadan.[27]

Discussion

Ramadan is an obligation that millions of Muslims worldwide observe. It is a month of the lunar year and thus it occurs at different times in consecutive years according to Gregorian calendar. As such Ramadan could fall in the winter where

**Table 1. Incidence of Cardiac Disease in Cardiac Patients.**

Author	Year	Country	Patient with	Number of Patients	Parameter Measured	Result
Al Suwaidi et al.[16]	2004	Qatar	Prior MI	238	Incidence of CHF	Less likely to be hospitalized for CHF during ramadan (25%) than a month before (33.5%), after (35.9%), and a 9month average (29.1%)(p<0.05)
			Hx Coronary Artery Bypass Surgery	86	Incidence of CHF	No statistically Significant Difernece in hospitalization for CHF between Ramadan (7.2%) a month before before ramadan (8.8%), after ramadan (9.6%), and a 9month average (9.7%).(p>0.05)
Al Suwaidi et al.[13]	2004	Qatar	Hx of AMI	75	Incidence of AMI	No statistically Significant Difernece one month before Ramadan (15%), During (19%) and after (19%)
			Hx Coronary Artery Bypass Surgery	59	Incidence of AMI	No statistically significant difference one month before Ramadan (3.2%), during (3.5%), and after (3%)
Al Suwaidi et al.[17]	2005	Gulf Countries	Cardiac Disease (general not specified)	465	Comfort and incidence of Cardiac Events	27% felt better, 6.7% felt worse, 4.5% developed cardiac events.
Bener et al. [18]	2006	Qatar	AMI	201	Hospitalization for Stroke	No statistically Significant Difernece (53.3% of stroke patients had AMI before ramadan, 62% during, and 69% after)
Comoglu et al. [20]	2003	Turkey	Cardiac Disease (general not specified)	319	Hospitalization for Stroke	No statistically Significant Difernece (41.1% of stroke patients had a Cardiac Disease before ramadan, 42.5% during, and 37.5% after)
Chamsi-Pasha et al. [19]	2004	Saudi Arabia	Cardiac Disease (general not specified)	86	Hospitalization	Non Required
			Cardiac Disease (general not specified)	86	NYHA Class	No Significant Change During Fast (mean class: 1.4 before Ramadan, 1.2 after, p=0.12)
			Coronary Artery Disease	46	NYHA Class	No Significant Change During Fast (mean class: 1.2 before Ramadan, 1.1 after, p=0.57)
El Mitwalli et al.[21]	2010	Egypt	Cardiac Disease (general not specified)	138	Stroke Admissions	No statistically Significant Difernece (30.2% of stroke patients had a Cardiac Disease before ramadan, 24.1% during, p=0.1)
Mousavi et al. [24]	2014	Iran	CAD	148	Chest Pain and Dyspnea	No statistically significant difference in incidence of chest pain or dyspnea between fasting and non fasting groups (P = 0.141, OR = 0.416, and 95% CI, 0.126-1.374)
Salam et al [22]	2013	Qatar	Prior MI	236	Hospitliization for Afib	Less likely to be hospitalized for Afib during Ramadan (9.1% of Afib Patients had prior MI before Ramadan, 9.8% during, 23.2% after p=0.02)
			Previous HF	133	Hospitliization for Afib	No Significant Difference (22.1% of Afib Patients had prior HF before Ramadan, 20.3% during, 36.5% After,p=0.6)
			Valvular Heart Disease	14	Hospitliization for Afib	No Significant Difference (2.9% of Afib Patients had prior Valvular disease before Ramadan, 3.5% during, 1.3% After,p=0.45)
			AMI	37	Hospitliization for Afib	No Significant Difference (9% of Afib Patients had prior HF before Ramadan, 3.5% during, 7.3% After,p=0.21)
Salam et al [23]	2017	Gulf Countries	Known Systolic LV dysfunction	1919	Hospitalization for HF	No statistically Significant Difernece (46.4% of HF patients had Systolic LV dysfunction during Ramadan, 46.1% in non-Ramadan months,p=0.93)
			Known CAD	1928	Hospitalization for HF	Admitted patients were more likely to have CAD prior (54.6% of HF patients had prior CAD during Ramadan, 47.1% in non Ramadan Months,p=0.01)
			Congenital Heart Disease	32	Hospitalization for HF	No statistically Significant Difernece (0.3% of HF patients had congenital disease during Ramadan, 0.8% in non-Ramadan months , p=0.36)
			Valvular Heart Disease	578	Hospitalization for HF	No statistically Significant Difernece (12.7% of HF patients had valvular disease during Ramadan, 14% in non-Ramadan months,p=0.54)

Table 2. Cardiovascular Risk Parameters in Cardiac Patients

Author	Year	Country	Sample Size	Parameters Measured	Results
Chamsi Pasha et al. [19]	2004	Saudi Arabia	86	Hematologic and Biochemical Parameters	No significant Change during the fast (all p>0.05)
Khafaji et al. [26]	2011	Qatar	56	TC,TG,HDL-C,LDL-C,hs-CRP,Serum Leptin in stable cardiac patients	TC (5.35 ± 0.99 to 5.58 ± 0.99),TG (2.06 ± 0.94 to 2.21 ± 1.56),hs-CRP (0.90 ± 1.84 to 0.57 ± 0.46),Leptin (12.25 ± 10.52 to 12.71 ± 10.58): no significant change; HDL-C dec significantly (1.12 ± 0.24 to 1.05 ± 0.25; P = 0.012); LDL-C inc. significantly (3.31 ± 0.97 to 3.59 ± 0.92; P = 0.022) during fasting
Nematy et al.[27]	2012	Iran	82	10 year coronary heart disease risk, Lipids Profile, BP, FBS, insulin, HOMA-IR, hcy, hs-CRP in patients with previous Cardiovascular Disease	Improvement in 10 year coronary heart disease risk (13.0 ± 8 before Ramadan and 10.8 ± 7 after Ramadan, P <0.001), total cholesterol, triglycerides, VLDL-c, LDL-c, cholesterol/HDL and LDL/HDL ratio were significantly decreased (P = 0.02 for cholesterol and P <0.001 for rest) and HDL-c increased significantly (P <0.001); dec. in SBP (132.9 ± 16 mmHg vs 129.9 ± 17 mmHg, P = 0.03); no change in DBP (80.2 ± 9 vs 78.6 ± 11 mmHg, P = 0.14); no significant change in FBS, insulin, HOMA-IR, hcy, hs-CRP (P = 0.33, P = 0.58, P = 0.76, P = 0.06 and P = 0.07 respectively)
Yousefi et al. [25]	2014	Iran	21	NO,ADMA,VEGF,MDA,TG,HDL-C,TC/HDL-C,FBS,TC, LDL in patients with previous cardiovascular disease	Significant inc. of NO (85.1 ± 11.54 vs 75.8 ± 10.7 µmol/l, P=0.011); Significant dec of ADMA (802.6 ± 60.9 vs 837.6 ± 51.0 nmol/l, P=0.034); Insignificant dec. of MDA (3.2 ± 0.7 vs 3.6 ± 1.1 µmol/l,P=0.329); Insignificant inc. of VEGF (228.1 ± 27.1 vs 222.7 ± 22.9 pg/ml,P=0.122); Significant dec. of TG (176±56 vs 148± 52 mg/dl,P=0.018), TC (186±43 vs 175± 35 mg/dl,P=0.062), TC/HDL-C ratio (4.76±1.52 vs 4.01±1.49,P<0.001); Significant inc. of HDL-C (40±14 vs 46±13 mg/dl,P<0.001); No significant change in FBS (112±42 vs 118± 38 mg/dl P=0.091),TC (186±43 vs 175± 35 mg/dl,P=0.062) and LDL-C (115±31 vs 109± 39 mg/dl,P=0.11)

SBP: Systolic Blood Pressure, **DBP:** Diastolic Blood Pressure, **PP:** Pulse Pressure, **TG:** Triglyceride, **TC:** Total Cholesterol, **GSH:** Glutathione, **ADMA:** Asymmetric Dimethyl Arginine, **MDA:** Malonylaldehyde, **FBS:** Fasting Blood Sugar, **HOMA-IR:** Homeostatic Model Assesment for Insulin Resistance, **Hcy:** Homocystein, **NO:** Nitric Oxide, **VEGF:** Vascular Endothelial Growth Factor, **HR:** Heart Rate, **Dec:** Decrease, **Inc:** Increase

daylight hours are short, or it could fall in the summer where the fasting hours could reach up to 18 hours depending on the geographical location. These long fasting hours will require rescheduling of medication time and adequate fluid intake. Most studies have shown that Ramadan fasting has no adverse effects on incidence of various cardiovascular diseases, or the number of hospitalizations due to cardiac disease events.

An important exception to this is that patients with chronic kidney disease (GFR< 30/min/1.73 m2) would be advised not to fast. Those with early stage CKD (GFR> 30 ml/min/ 1.73 m2) could fast after a trial of few days and documenting no increase in creatinine levels. Patients would be advised to increase the fluid intake between Iftar and Suhur.

The studies above have been done in different countries and have thus assessed different populations and socioeconomic classes. Cultures and sub-cultures differ in their dietary habits during Ramadan. Different populations and classes are bound to have differences in the type of foods consumed during Ramadan. For example, eating habits in Morocco are not usually present in countries like Iran and Kuwait. Measures taken by physicians to avoid health risks during Ramadan must therefore come after careful examination of the lifestyle and eating habits of the patients.

It is important to note the effects of fasting on hypertension since hypertension is well known risk factor for cardiovascular events. Some studies showed a decrease in blood pressure during fasting,[20, 28, 29] but Topacoglu et al reported an increase in the number of admissions for hypertension to the ED during Ramadan.[30] The discrepancies can be explained by the following; amelioration in blood pressure can be due to dehydration effects during long fasting time.[28] It can also be attributed to decreasing day time activity which leads to a decrease in sympathetic tone.[31] Chamsi-Pasha et al advise avoiding diuretics during fasting specially when fasting days are hot and long, or administering them in the evening.[32] According to this, hypertensive patients can fast but should pay attention to meals they might take that might raise their blood pressure abruptly, as can be concluded by the rise of blood pressure after morning meals reported by Khafaji et al.[26]

The effect of Ramadan fasting on patients with Coronary Artery Disease was shown to be somewhat protective with regard to incidence of CHF,[16] or Afib.[22] However, Salam et al reported in a recent large sample size study, a higher likelihood that patients admitted for HF during Ramadan have prior CAD.[23] Even though both studies regarding HF we done in the same country, the differences in results between these two studies on HF hospitalization in CAD patients may be attributed to the

Table 3. NIH Quality Assessment tool Ratings

Study	Year	Quality Rating
Al Suwaidi et al.	2004	Good
Al Suwaidi et al.	2004	Good
Al Suwaidi et al.	2005	Good
Bener et al.	2006	Good
Comoglu et al.	2003	Fair
Chamsi Pasha et al.	2004	Good
El Mitwalli et al.	2010	Good
Mousavi et al.	2014	Fair
Salam et al.	2013	Good
Salam et al.	2017	Good
Khafaji et al.	2011	Fair
Nematy et al.	2012	Fair
Yousefi et al.	2014	Poor

difference in sample size, whereby the large sample size (1928 patients with CAD) in the study reported by Salam et al. might bring higher statistical reliability and generalizability. These three studies did not directly assess whether a participant did fast or not, but relied on the cultural norm of their respective societies that most participants would have fasted. This could be a limitation in the methodology of these studies since the exposure under study was not measured accurately but estimated.

Only Khafaji et al reported a deterioration in lipid profile during Ramadan (decrease in HDL and increase in LDL).[26] An elevation in LDL and a decrease in HDL; a characteristic of hypercholesterolemia is an important risk factor for atherosclerosis in CAD. However, Salim et al attributed this to the timing of blood sample extraction which was at closer to the time of the last meal in Ramadan than that in non- fasting months. [33] Some studies in healthy individuals show amelioration or no significant changes of lipid profiles in Ramadan. These studies also report elevation in HDL levels.[34-36] Other studies indicated an increase in LDL and TC levels.[37, 38] The results of studies regarding lipid profiles are thus contradictory, and are based on small sample sizes which could limit their reliability. Part of the contradiction can be due to the difference in dietary composition, eating habits, and physical activity between different populations and countries. According to the specific culture patients belong to, high fat diets might be common at the breaking of fast meals. Thus, patients with CAD are advised as a precaution to decrease cholesterol and saturated fatty acid (SFA) intake in their diet, as high levels of SFA are associated with increased TC and LDL levels. They are also advised to increase consumption of mono-unsaturated fatty acids (MUFA) found mostly in vegetable oils. MUFA are known to decrease the risk of CAD as evident by the decrease of CAD in Mediterranean cultures.[34] These patients are also advised to strictly abide by medications controlling

their lipid profiles, hypertension or hyperglycemia. They are also advised to achieve the highest possible health benefits of Ramadan fasting and avoiding any risks.

Though Salam et al. studied hospitalization for atrial fibrillation patients with previous myocardial infarction[23], the literature is lacking with studies on patients with arrhythmias during Ramadan fasting. In our search, no study included arrhythmic patients except the case report on a patient with diagnosed Brugada syndrome.[14]

Studies on cardiac risk factors in cardiac patients during Ramadan showed that fasting does not increase the risk of complications. As tabulated above, some showed no significant change in risk factors while others showed amelioration in cardiac risk factors. C-reactive protein (CRP) has been correlated with acute coronary events. Leptin has a vasoactive and prothrombic role, and it can increase with acute myocardial infarction.[26] High homocysteine levels are risk factors for cardiovascular disease and affect the vascular wall and the coagulation system.[35] Nitric oxide (NO) mediates the functions of vascular endothelial growth factor (VEGF), which in turn stimulates angiogenesis, vasodilation, and vascular permeability. Asymmetric dimethylarginine (ADMA) reduces NO production and is thus an important risk factor for cardiovascular disease. Plasma malondialdehyde (MDA) is a determinant of oxidative stress and is shown to increase in level in cardiovascular disease.[25] These studies remain small studies with small sample sizes. Larger studies are needed to establish a clearer relation.

Studies on HF patients are scarce. Salam et. al reported no significant change in hospitalization in patients with previous HF during the month of Ramadan.[23] Though one other study showed no significant change in CHF incidence during Ramadan, precautions have to be undertaken by patients with previous heart failure to minimize the risk of recurrence during Ramadan due to harsh fasting conditions, and possible change in eating habits. [16] Controlling hypertension and dyslipidemia is important especially in the setting of CAD. Patients with hypertension on a twice per day regimen will require rescheduling the medications from the morning and evening to the Iftar and Suhur.

Studies regarding Ramadan fasting and cardiovascular disease are relatively scarce. Also different findings between populations are expected because of the differences in geography, climate, fasting and breaking fast traditions, health, activity and fitness levels of the study populations. Though many show amelioration or no significant effect of Ramadan fasting on cardiovascular health, cardiac patients should be closely monitored during Ramadan. Since there cannot be conclusive generalized evidence from the studies present at hand regarding any adverse effects Ramadan fasting could have on health cardiac patients, some precautions should be taken. Patients must frequently visit their doctors to check for any signs of complication. They must strictly adhere to any medication prescribed though its schedule is shifted. This medication should also be evaluated for any effects that might lead to hypoglycemia, dehydration, or hypotension as no food nor drink is consumed for long hours that can reach up to 18 hours depending on location and season. Medication or diet could be changed as an adaptation for the change of lifestyle. All cardiac patients are also advised to drink

lots of fluid during non-fasting times, and adhere to a strict low fat, low cholesterol diet. Physical activity is also strongly advised but within the limit of personal physical ability.

Special attention should be made to diabetic patients, specifically those with previous stroke incidences, as they should be closely monitored during the fast. They should strictly follow a diet and exercise regime.[33] High blood pressure, smoking, abdominal obesity, diet and lack of physical activity are risk factors that may increase the recurrence of stroke.[39] Uncontrolled FBS may also lead to cardiac disease complications in diabetic patients. Diet is important in these patients to improve glycaemia stability and reduce atherogenic risk. These patients are also advised to monitor their blood pressure, adhere to prescribed hypertensive medication, monitor their diet and engage in physical exercise.

Well-controlled patients with diabetes mellitus (DM) treated with lifestyle therapy, metformin, acarbose, sulfonylurea, thiazolidinediones, incretin-based therapies and/or short-acting insulin secretagogues, and that are otherwise healthy, can fast in Ramadan.[40] Patients with diabetes on oral hypoglycemic will require adjustments of the doses: the metformin dose that is given three times daily should be changed to twice daily with two-thirds of the dose at the sunset meal and one third of the dose at the predawn meal. If a sulfonylurea is given twice a day, half of the usual morning dose is given at the predawn meal and the usual dose at the sunset meal. No change is needed for thiazolidinedione, alpha-glucosidase inhibitor or incretin-based therapies dosages. If patients are having premixed or intermediate-acting insulin twice daily, the regimen should be changed to long-acting or intermediate insulin in the evening with short or rapid-acting insulin with meals (usual dose at sunset and half usual dose at predawn meal).[40] The Epidemiology of Diabetes and Ramadan (EPIDIAR) study showed increased hypoglycemia in patients with type 1 DM (4.7 fold) and type 2 DM (7.5 fold).[41] However, the Ramadan Education and Awareness in Diabetes (READ) study showed that hypoglycemic episodes during Ramadan in patients with type 2 Diabetes Mellitus was associated with no Ramadan-focused diabetes education.[42] Diabetic patients with a HbA1c of more than 10%, recurrent hypoglycemic episodes, acute illness, type 1 diabetes, or who engage in intense physical labor or are pregnant, are advised not to fast. [43]

One limitation of this review is the exclusive search for studies published in the literature. If any investigators did not publish negative results, their studies would have been missed by the search strategy for this review. The inclusion of results from articles that were not the main outcomes of their respective studies protects against this bias.

Conclusions

Patients with stable controlled cardiac disease may fast during the month of Ramadan since most studies show no significant adverse effect of fasting on these patients. Physician consultation and monitoring is highly advised in these patients before and during the fast. Adhering to prescribed medications, a strict diet, drinking fluids and increasing physical activity is highly advised. Diabetic and hypertensive patients with stable cardiac disease must be monitored closely and must commit to controlling glycemia, blood pressure, and lipid levels during the fast.

Declarations of Interest

The authors declare no conflict of interest.

Acknowledgments

The authors state that they abide by the authors' responsibilities and ethical publishing guidelines of the International Cardiovascular Forum Journal [44].

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