Ramadan fasting: recommendations for patients with cardiovascular disease

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Mohammed Yunus Khanji1,11,12,13

ABSTRACT

Ramadan fasting is observed by most of the 1.8 billion Muslims around the world. It lasts for 1 month per the lunar calendar year and is the abstention from any food and drink from dawn to sunset. While recommendations on ‘safe’ fasting exist for patients with some chronic conditions, such as diabetes mellitus, guidance for patients with cardiovascular disease is lacking. We reviewed the literature to help healthcare professionals educate, discuss and manage patients with cardiovascular conditions, who are considering fasting. Studies on the safety of Ramadan fasting in patients with cardiac disease are sparse, observational, of small sample size and have short follow-up. Using expert consensus and a recognised framework, we risk stratified patients into ‘low or moderate risk’, for example, stable angina or non-severe heart failure; ‘high risk’, for example, poorly controlled arrhythmias or recent myocardial infarction; and ‘very high risk’, for example, advanced heart failure. The ‘low–moderate risk’ group may fast, provided their medications and clinical conditions allow. The ‘high’ or ‘very high risk’ groups should not fast and may consider safe alternatives such as non-consecutive fasts or fasting shorter days, for example, during winter. All patients who are fasting should be educated before Ramadan on their risk and management (including the risk of dehydration, fluid overload and terminating the fast if they become unwell) and reviewed after Ramadan to reassess their risk status and condition. Further studies to clarify the benefits and risks of fasting on the cardiovascular system in patients with different cardiovascular conditions should help refine these recommendations.

INTRODUCTION

There are approximately 1.8 billion Muslims in the world and 3.4 million Muslims in the UK, 93% of whom are likely to observe Ramadan fasting. With a significantly high and increasing prevalence of cardiovascular disease in Muslim communities, including the UK, healthcare professionals (HCPs) are likely to come across requests from patients asking for their suitability for Ramadan fasting.

Adult Muslims are obligated to fast during the month of Ramadan if it is safe to do so (see table 1 for fasting in major religions). Ramadan fasting is the abstention of all food and drink from dawn until sunset. Taking medicines orally or intranasally is considered breaking one’s fast. Outside of the pre-dawn to sunset window, Muslims can eat, drink and take medications as normal. In a typical fast, Muslims have a pre-dawn meal (termed ‘suhoor’) and a meal at sunset to break their fast (termed ‘iftaar’). An Islamic lunar month can be 29 or 30 days and falls 11 days earlier each year compared with the Gregorian solar calendar. In temperate regions, when Ramadan falls in the winter, fasts are shorter. Conversely, summer fasts in some countries can be as long as 20 hours per day.

Exemptions to Ramadan fasting exist for individuals whose health may come to significant harm from it. Groups such as the frail elderly and those with significant mental and/or physical health illness are exempt from fasting. Muslims are permitted to break their fast if they become unwell and can make up their fast if and when they fully recover. If Muslims are in doubt about their obligation to fast with respect to their medical condition, they are encouraged to consult with their HCPs and their local Islamic scholar. Many individuals who have been advised not to fast by their HCP may still choose to do so.

Due to the absence of randomised controlled trials, guidelines or expert statements on the management of patients with cardiovascular disease who wish to undertake Ramadan fasting, we undertook a narrative review of the existing literature to underpin guidance for HCPs managing patients with cardiovascular conditions desiring to fast in Ramadan. Our work builds on a limited survey of the literature with brief recommendations by the authors of this manuscript, on behalf of the British Islamic Medical Association.

Patients with cardiovascular disease frequently have comorbidities such as diabetes mellitus (DM) and chronic kidney disease (CKD). These conditions can interact with cardiovascular disease, such as iatrogenic hypoglycaemia triggering arrhythmias in a patient with DM. Therefore, it is essential to take a holistic approach when advising patients with cardiac disease undertaking Ramadan fasting. Guidance on managing patients with DM, epilepsy, adrenal insufficiency and CKD has recently been published.

METHODS

We identified publications in PubMed and Embase using the following predefined terms in various combinations: ‘intermittent fasting’, ‘fasting’, ‘Ramadan’, ‘restricted feeding’, ‘cardiovascular disease’, ‘atrial fibrillation’, ‘hypertension’, ‘channelopathies’, ‘cardiomyopathy’ and ‘valvular heart disease’. We included studies that examined ‘intermittent fasting’ to broaden our evidence base, although we appreciate that some forms of intermittent fasting differ from Ramadan fasting, particularly with regard to water fasting.
We used any relevant studies, our clinical experience of managing Muslim patients fasting in Ramadan and the well-established International Diabetes Federation and the Diabetes and Ramadan International Alliance (IDF-DAR) risk stratification model\(^\text{16}\) to form a consensus statement and provide risk stratification and management recommendations for safe fasting. Although the more recently published IDF-DAR Ramadan guidelines\(^\text{14}\) introduce a scoring system, this has not been validated and is based on physician opinion derived from an online survey with a limited evidence base. As this is a very new introduction, even from a diabetes perspective, it is not known if it is better than the previous risk stratification.\(^\text{17}\) We therefore relied on their well-established risk stratification model, but as more evidence emerges in this area, a scoring system could...
be considered. Table 2 can therefore be used by HCPs to risk stratify patients with cardiovascular disease desiring to fast in Ramadan and provide appropriate advice.

What therapies and factors need to be taken into consideration in patients with cardiovascular conditions
Fasting-associated dehydration may lead to electrolyte abnormalities which could be life-threatening in patients with unstable arrhythmias, inherited arrhythmia syndromes (eg, long QT or Brugada syndrome), or on medications such as class Ic antiarrhythmics, digoxin and renin–angiotensin–aldosterone antagonists. Many cardiac medications can induce hypotension, potentially precipitating syncope, particularly in elderly patients with impaired baroreflexes. This may be exacerbated by dehydration or a shortened interval between a bedtime and breakfast dose if medication dosing is altered by patients trying to facilitate fasting.

Aslam and Healy found 42% of the 81 Southeast Asian Muslim patients they surveyed were adherent to their usual treatment schedule in Ramadan, possibly because of a disruption in their routine as a result of fasting. In patients taking antiplatelets for coronary stent implantation or anticoagulation for stroke prevention in atrial fibrillation, medication non-compliance may be fatal.

Summary of the key studies examining fasting and cardiovascular disease
Hypertension
In a prospective observational study by Aslan et al assessing the safety of diuretic therapy in patients with hypertension, Ramadan fasting appeared to significantly decrease systolic and diastolic blood pressures in individuals using diuretics, which was well tolerated without complication. Eldeeb et al noted improved blood pressure control in patients with hypertension, irrespective of renal function, and improved arterial compliance in those without CKD, in patients undertaking Ramadan fasting.

Chronic coronary syndrome
In an observational study of patients with chronic coronary syndrome (CCS), as defined by the European Society of Cardiology (ESC), Khafaji et al reported that Ramadan fasting was not associated with an increased cardiac mortality or morbidity, with 29% of patients reporting improved cardiac symptoms. Similar findings were seen by Mousavi et al in patients with CCS and a normal left ventricular function.

Acute coronary syndrome
Temizhan et al compared the incidence of acute coronary syndrome (ACS), as defined by the ESC, in 1655 patients at a single centre, in the month before, during and after Ramadan, over a 6-year period. They noted no significant differences in the incidence of ACS in Ramadan when compared with the preceding or following month. A multicentre study by Amin and Alaraag demonstrated that patients who undertook Ramadan fasting within 3 months of percutaneous coronary intervention had a higher incidence of significant cardiac events than those who did not undertake Ramadan fasting.

Heart failure
Abazid et al in an observational study, demonstrated that 92% of patients with heart failure with a reduced ejection fraction (HFrEF) (left ventricular ejection fraction (LVEF) ≤40%) with ‘close monitoring’ did not experience worsening HF symptoms. Patients with a non-ischaemic cardiomyopathy and/or a history of non-compliance with fluid restrictions and/or medications were more likely to experience worsening HF symptoms. A retrospective review of more than 2000 patients hospitalised with HFrEF over a 10-year period found no increase in the number of HF hospitalisations in Ramadan when compared with other months in the year.

An expert panel examined the safety of sodium–glucose cotransporter 2 inhibitors (SGLT2i) in patients observing Ramadan fasting and agreed on the following: SGLT2i should be initiated at low dose, in the evening and at least 1 month before Ramadan; fluid intake should be increased during non-fasting hours; hypoglycaemia should be avoided by reviewing any concomitant medications for type 2 DM and SGLT2i should be avoided in the elderly, patients with CKD or those receiving loop diuretics.

Arrhythmias
Disrupted cellular metabolism and ion channel function can result in cardiac arrhythmias. Kahraman and Dogan report a asymptomatic high burden of premature ventricular complexes in a patient undertaking Ramadan fasting, with recurrences only in subsequent attempts at Ramadan fasting, on further monitoring. The ESC 2020 sports cardiology advises that patients with long QT syndrome should carefully avoid dehydration. American Heart Association guidelines state that sleep cycle and eating disturbances, common in Ramadan fasting, could lead to an increased incidence of atrial fibrillation. A multi-centre cross-sectional study by Batarb et al surveyed a cohort of 809 patients undertaking Ramadan fasting and receiving oral anticoagulation: 68.4% of patients received warfarin, the remaining received direct oral anticoagulants (DOACs); of these 50% modified their anticoagulation regimen (intake time, skipped doses, drugs being taken at the same time two times per day) without prior consultation with their physician. Patients receiving two times per day DOACs were noted to be more likely to change their anticoagulation administration and more likely to be admitted to hospital with a consequence of their changes, for example, bleeding or stroke.

Other cardiovascular conditions
The 2014 ESC and 2020 American College of Cardiology guidelines for hypertrophic obstructive cardiomyopathy (HOCM) recommend that patients should remain well hydrated to reduce the occurrence of potentially life-threatening symptoms such as syncope. Likewise, the 2020 ESC guidelines for patients with adult congenital heart disease (ACHD) also recommend avoiding dehydration in patients with ACHD, particularly cyanotic ACHD. Dehydration is also noted as a risk factor for the recurrence of orthostatic intolerance syndromes, including neurogenic and non-neurogenic orthostatic hypotension and postural orthostatic tachycardia syndrome.

Summary of the evidence
The available studies state that with ‘close monitoring’, fasting may be safely undertaken in patients with CCS or HFrEF. There are very few if no published data on Ramadan fasting in other forms of cardiovascular disease, including cardiomyopathies, arrhythmias or valvular heart disease. The published data on Ramadan fasting are weak, are observational, lack a large sample size with sufficient power, have prolonged follow-up beyond the month of Ramadan, do not clearly define what ‘close monitoring’ means or have detailed information about the diet of the


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patients outside of their fast (see our online supplemental index for a summary of the studies highlighted in our review). This point is echoed by Santos and Macedo in their narrative review of the published data on intermittent fasting on lipid profile. General recommendations based on the available evidence

Patients with cardiac conditions desiring to fast in Ramadan should be assessed on an individual basis, by their HCP, during a routine consultation before Ramadan. In table 2, we risk stratify patients according to their cardiac conditions, although some patients deemed ‘low-moderate’ risk for fasting may be at higher risk in view of specific features of their conditions or their comorbidities. In figure 1, we provide a proposed pathway for HCPs managing a fasting patient with cardiac disease. At present, we are not able to provide guidance on the combination of low-moderate risk conditions, whether these are purely cardiovascular or combined with non-cardiac conditions as is frequently the case. Figure 2 provides a suggested consultation checklist for HCPs managing patients with cardiovascular disease desiring to fast in Ramadan.

Table 3 summarises the risks associated with different classes of cardiac medications and their use while fasting in Ramadan. In a review in the Canadian Pharmacists Journal, Grindrod and Alsabbagh suggested that if medication adjustments are made to facilitate fasting, strategies could include choosing once-daily medications or long-acting formulations where safe and appropriate to do so and without compromising the treatment offered. When initiating new medication in patients who may wish to fast, once a day dosing of medication should be considered, particularly where safety and efficacy is equivalent to medication with more frequent daily dosing. For patients on established therapies, we would suggest avoiding medication changes where possible.

The following points should be considered when advising patients who wish to fast, although all recommendations should take into consideration the climate, country and season where the patient is fasting:

Hypertension

Blood pressure, kidney function and medications (particularly antihypertensives that have a diuretic component such as aldosterone antagonists or thiazide-like diuretics) should be reviewed by HCPs during a routine appointment to reduce the risk of hypotension and/or worsening kidney function. A home blood
Table 3  Summary of the potential risks that could occur with different classes of cardiac medication used while fasting (reproduced based on10, with permission)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Condition used in</th>
<th>Risk in fasting</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACE inhibitor (e.g., ramipril)</td>
<td>Hypertension</td>
<td>May worsen fasting-associated hypotension, which may result in dizziness or loss of consciousness. May compound fasting-associated dehydration resulting in an acute kidney injury and/or life-threatening electrolyte abnormalities, for example, hyperkalaemia. Medication non-compliance may result in uncontrolled hypertension, decompensated heart failure.</td>
</tr>
<tr>
<td>Aldosterone receptor blockers (e.g., candesartan)</td>
<td>Heart failure</td>
<td></td>
</tr>
<tr>
<td>Angiotensin receptor nephrilisin inhibitor (ie, sacubitril/valsartan)</td>
<td>Coronary artery disease/myocardial infarction</td>
<td>Medication non-compliance can increase risk of acute stent thrombosis, myocardial infarction and death if antplatelets are not taken regularly—particularly in patients with recent coronary stent implantation (&lt;6 months). Ticagrelor is taken two times per day and has a half-life of 7 hours (see above section on taking medications more than 12 hours apart and the effect it may have).</td>
</tr>
<tr>
<td>Antiplatelet medications (e.g., aspirin, clopidogrel, prasugrel, ticagrelor)</td>
<td>Risk in fasting</td>
<td></td>
</tr>
<tr>
<td>Antithrombin (AAs) (eg, amiodarone, flecainide, sotalol)</td>
<td>Atrial tachyarrhythmias Ventricular tachyarrhythmias</td>
<td>Some may worsen fasting-associated hypotension, which may result in dizziness or loss of consciousness. Fasting-associated dehydration may result in significant electrolyte abnormalities that may increase risk of AAD toxicity.</td>
</tr>
<tr>
<td>Beta blockers (e.g., bisoprolol)</td>
<td>Hypertension</td>
<td>May worsen fasting-associated hypotension, which may result in dizziness or loss of consciousness. Medication non-compliance may result in worsening angina, decompensated heart failure, more frequent arrhythmias.</td>
</tr>
<tr>
<td>Calcium channel blockers (e.g., amlopidine, diltiazem)</td>
<td>Coronary artery disease Arhythmias Hypertension</td>
<td>May worsen fasting-associated hypotension, which may result in dizziness or loss of consciousness. Medication non-compliance may result in worsening angina, more frequent arrhythmias, uncontrolled hypertension.</td>
</tr>
<tr>
<td>Cardiac glycosides (e.g., digoxin)</td>
<td>Hypertension</td>
<td>Digoxin toxicity may occur in potential case of fasting-related acute kidney injury.</td>
</tr>
<tr>
<td>Direct oral anticoagulants (DOACs) (eg, apixaban, rivaroxaban, edoxaban)</td>
<td>Atrial flutter/atrial fibrillation Deep venous thrombosis/pulmonary embolism</td>
<td>Two times per day DOACs: The half-life of apixaban is 12 hours—if taken early morning, for example, 03:00 (Suhoor) and then again at, for example, 20:00 (Iftaar), there may be a period in between where the patient is not adequately anticoagulated. Medication non-compliance may result in stroke or death.</td>
</tr>
<tr>
<td>Immunosuppressant therapy (e.g., tacrolimus)</td>
<td>Heart transplant</td>
<td>May compound fasting-associated dehydration and result in an acute kidney injury and/or life-threatening electrolyte abnormalities, for example, hyperkalaemia. Medication non-compliance may result in organ rejection and death. Tacrolimus is taken two times per day and therefore care must be taken to avoid long periods in between.</td>
</tr>
<tr>
<td>Loop diuretics (e.g., furosemide, bumetanide)</td>
<td>Hypertension Heart failure</td>
<td>May worsen fasting-associated hypotension, which may result in dizziness or loss of consciousness. May worsen fasting-associated dehydration resulting in an acute kidney injury and/or life-threatening electrolyte abnormalities, for example, hyperkalaemia. Medication non-compliance may result in uncontrolled hypertension, decompensated heart failure.</td>
</tr>
<tr>
<td>Thiazide diuretics (e.g., bendroflumethiazide)</td>
<td>Hypertension Heart failure</td>
<td></td>
</tr>
<tr>
<td>Mineralocorticoid receptor antagonists (e.g., spironolactone)</td>
<td>Hypertension Heart failure</td>
<td>May worsen fasting-associated hypotension, which may result in dizziness or loss of consciousness. May worsen fasting-associated dehydration resulting in an acute kidney injury and/or life-threatening electrolyte abnormalities, for example, hyperkalaemia. Medication non-compliance may result in uncontrolled hypertension, decompensated heart failure.</td>
</tr>
<tr>
<td>Phosphodiesterase type 5 inhibitors (e.g., sildenafil)</td>
<td>Pulmonary hypertension</td>
<td>May worsen fasting-associated hypotension, which may result in dizziness or loss of consciousness. May result in diarrhoea, worsening fasting-associated hypotension.</td>
</tr>
<tr>
<td>Prostanoids (e.g., epoprostenol)</td>
<td>Idiopathic pulmonary arterial hypertension</td>
<td>May worsen fasting-associated hypotension, which may result in dizziness or loss of consciousness.</td>
</tr>
<tr>
<td>Statins (e.g., atorvastatin)</td>
<td>Coronary artery disease/myocardial infarction</td>
<td>Fasting-associated dehydration may increase risk of acute kidney injury. This may compound a rare side effect of statins—rhabdomyolysis.</td>
</tr>
<tr>
<td>Sodium-glucose cotransporter 2 inhibitors (e.g., dapaglifozin)</td>
<td>Heart failure Diabetes mellitus</td>
<td>May worsen fasting-associated hypotension, which may result in dizziness or loss of consciousness. May worsen fasting-associated dehydration resulting in an acute kidney injury and/or life-threatening electrolyte abnormalities, for example, hyperkalaemia. Medication non-compliance may result in decompensated heart failure and cause/worsen hyperglycaemia in patients with diabetes mellitus.</td>
</tr>
<tr>
<td>Soluble guanylate cyclase inhibitors (e.g., vericiguat)</td>
<td>Heart failure</td>
<td>May worsen fasting-associated hypotension, which may result in dizziness or loss of consciousness.</td>
</tr>
<tr>
<td>Vasodilators: Long-acting nitrates (e.g., isosorbide mononitrate)</td>
<td>Hypertension Coronary artery disease Pulmonary hypertension</td>
<td>May worsen fasting-associated hypotension, which may result in dizziness or loss of consciousness.</td>
</tr>
</tbody>
</table>

Suhoor: pre-dawn meal before Muslims initiate fast; Iftaar: meal at sunset that breaks fast.

Medication changes may not be possible due to (1) significantly reduced outpatient consultations with specialists and/or GPs due to COVID-19; (2) a specialist may deem alternate medications to be less beneficial for a patient. Medication changes should be planned well in advance of Ramadan and should be discussed in a patient’s next routine appointment with their specialist, GP and or pharmacist or if a patient is ever admitted to the hospital under the care of the cardiology team.

GP, general practitioner.
pressure monitor would be useful to observe a patient’s blood pressure response to antihypertensive treatment while fasting and provide clarity on any symptoms that could suggest a low blood pressure. Patients with well-controlled blood pressure, as defined by their HCP, would be deemed ‘low-moderate’ risk for fasting.

CCS and ACS
The few studies in patients with CCS, whom we deem as ‘low-moderate risk’, undertaking Ramadan fasting suggest that is safe for them to do so, in line with guidance from the British Heart Foundation, and the ESC. We deem patients with severe (LVEF ≤35%) HFrEF and advanced HF, as defined by the ESC, as high and very high risk for Ramadan fasting, respectively. There are no studies investigating patients with HF with preserved ejection fraction (HFpEF) undergoing Ramadan fasting. We propose that stable patients with HFpEF, as defined by the ESC, are ‘low-moderate’ risk; however, each patient should be reviewed as particulars about their condition and/or their comorbidities may increase the risk, especially since HFpEF is a heterogeneous group.

Intracardiac devices
There are no studies assessing patients with pacemakers undertaking Ramadan fasting. We deem them to be ‘low-moderate’ risk provided they have no electrolyte abnormalities and their device clinic feels their device parameters are stable. Patients with cardiac resynchronisation therapy or implantable cardioverter defibrillators would be deemed at least ‘high risk’ as they are only indicated in patients with severe HFrEF and/or patients at significant risk of ventricular arrhythmias. We advise patients with intracardiac devices to inform their device clinic in their next device check of their desire to fast in Ramadan. A remote or in-person device check just before Ramadan would be ideal to ensure there are no issues that may prevent a patient fasting.

Others
Published studies examining the risk of Ramadan fasting in patients with atrial fibrillation, inherited arrhythmic syndromes, valvular heart disease, pulmonary hypertension, heart transplantation or ACHD are lacking. Ramadan fasting in pregnant women may be considered ‘moderate’ risk undertaking Ramadan fasting. The reviewed studies suggest that is safe for them to do so, in line with guidance for pregnant women with cardiovascular disease. There is a strong need for patients, HCPs and religious/community leaders to engage with each other and discuss these contemporary medical issues. Further studies are needed to explore gaps in knowledge around fasting and to help refine current recommendations.

CONCLUSION
The literature on Ramadan fasting in patients with cardiovascular disease is limited. Our review highlights the important role HCPs play in risk assessment, providing advice and education, encouraging medication compliance and monitoring to enable patients, where safe to do so, to fulfil their religious obligation while minimising the potential for harm. As patients with cardiovascular disease often have non-cardiac comorbidities, our recommendations should be used in combination with those for Ramadan fasting in non-cardiac conditions such as CKD, DM and epilepsy. There is a strong need for patients, HCPs and religious/community leaders to engage with each other and discuss these contemporary medical issues. Further studies are needed to explore gaps in knowledge around fasting and to help refine current recommendations.

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COVID-19-related cautions
If a patient is unwell with COVID-19, we advise against fasting. In a pandemic or in the post-pandemic phase, routine reviews by specialists or general practitioners, where patients could discuss their risk for Ramadan fasting, may not take place.

In these situations, we advise patients to adhere to professional advice or standard practice that they have received previously, provided there has not been a change in their clinical status that could increase their risk for fasting. Similarly, a bridge between taking an abstinence approach and not being able to access a clinician can be trial fasting in the weeks leading up to Ramadan. A patient’s previous experiences can also facilitate a clinician’s advice particularly if time is limited for a more thorough clinical assessment. It is worth noting however that many services, including blood test monitoring or community HF services, that may have facilitated fasting in Ramadan before, may not be available or available to a degree that allows patients to fast safely. Further discussion around fasting during COVID-19 is discussed elsewhere, but HCPs should bear these points in mind when risk stratifying their patient with cardiac disease for Ramadan fasting.

Heart failure
The few studies in patients with non-severe HFrEF, whom we would deem as ‘low-moderate’ risk undertaking Ramadan fasting suggest that is safe for them to do so, in line with guidance from the British Heart Foundation and the ESC. We deem patients with severe (LVEF ≤35%) HFrEF and advanced HF, as defined by the ESC, as high and very high risk for Ramadan fasting, respectively. There are no studies investigating patients with HF with preserved ejection fraction (HFpEF) undergoing Ramadan fasting. We propose that stable patients with HFpEF, as defined by the ESC, are ‘low-moderate’ risk; however, each patient should be reviewed as particulars about their condition and/or their comorbidities may increase the risk, especially since HFpEF is a heterogeneous group.

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Others
Published studies examining the risk of Ramadan fasting in patients with atrial fibrillation, inherited arrhythmic syndromes, valvular heart disease, pulmonary hypertension, heart transplantation or ACHD are lacking. Ramadan fasting in pregnant women may be considered ‘moderate’ risk undergoing Ramadan fasting. The reviewed studies suggest that is safe for them to do so, in line with guidance for pregnant women with cardiovascular disease. There is a strong need for patients, HCPs and religious/community leaders to engage with each other and discuss these contemporary medical issues. Further studies are needed to explore gaps in knowledge around fasting and to help refine current recommendations.

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7Department of Neuroscience, Imaging and Clinical Sciences, Institute of Advanced Biomedical Technologies, University of Genoa, Chieti Pescara, Abruzzo, Italy

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Review


43 Ponikowski P, Voors AA, Anker SD, et al. 2016 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure: the task force for the diagnosis and treatment of acute and chronic heart failure of the European Society of cardiology (ESC), developed with the special contribution of the heart failure association (HFA) of the ESC. *Eur J Heart Fail* 2016;18:891–975.


**Supplementary index**

**Table 1: Summary of relevant studies cited in our paper**

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<tr>
<th>Study authors</th>
<th>Study design</th>
<th>Cardiac condition</th>
<th>Number of patients</th>
<th>Type of fasting</th>
<th>Study objective</th>
<th>Follow up duration</th>
<th>Main findings</th>
<th>Conclusion</th>
</tr>
</thead>
</table>
| Abazid et al 2018      | Prospective nonrandomised study   | HFrEF            | 249                | Ramadan fasting | % of patients who became haemodynamically unstable and their clinical profile | 1 month (Ramadan)  | -92% of patients remained haemodynamically stable  
-Profile of patients who became haemodynamically unstable:  
--higher initial NYHA class (2.19±0.9 vs. 1.6±0.8)  
--less adherence to medications (67% vs 94%)  
--less likely to have ischaemic cardiomyopathy (33% vs 57%) | “In most patients with chronic HFrEF, Ramadan fasting is considered safe. Non-adherence to medication and diet are significantly associated with decompensated heart failure during Ramadan” |
| Al Suwaidi et al 2005  | Retrospective review population-based study | HFrEF             | 20,856 Qatari      | Ramadan fasting | Whether Ramadan fasting has any effect on the number of hospitalisations for HFrEF in a geographically defined population | Records over a 10-year period were reviewed (January 1991 to December 2001)  | -The number of hospitalisations for HFrEF was not significantly different in Ramadan (208 cases) when compared to a month before Ramadan (182 cases) and a month after Ramadan (198 cases) p>0.37.  
-There was no significant difference found in the baseline clinical characteristics or mortality (11.5%, 7.7% and 9.6%, respectively; p=0.43) in patients presenting in various time periods. | In this defined population, no significant difference was found in number of hospitalisations for HFrEF while fasting in Ramadan when compared to non-fasting months |
| Aslam M and Healy MA 1986 | Prospective review               | Not specified. 81 out of 81 had cardiac conditions. | 81 Asian           | Ramadan fasting | Medication compliance during Ramadan fasting | 1 month (Ramadan) | -35 patients missed doses  
-8 patients took their tablets at different times  
-4 patients took all their medication as one single daily dose while breaking their fast in the evening | Medication noncompliance remains a significant problem with patients fasting in Ramadan |
| Babineaux SM et al 2015 | Multi-country, retrospective, observational study | Type 2 Diabetes Mellitus | 3777 patients 508 physicians | Ramadan fasting | To describe the characteristics and management of patients with diabetes who chose to fast in Ramadan in 2010 | 73 months | -Oral antihyperglycemic therapy was the predominant pre-Ramadan therapy for most patients (76.6%)  
-Treatment regimen was modified before Ramadan for 39.3% of all patients  
-Almost all physicians (96.2%) reported provided fasting-specific advice to patients  
-62.6% of physicians report using guidelines or recommendations for the management of diabetes during Ramadan | Physicians have increasingly adopted multiple approaches to the management of fasting during Ramadan, including the adoption of international and/or national guidelines, such that patients are able to fast for a greater number of days without acute complications. |
<table>
<thead>
<tr>
<th>Study</th>
<th>Study Type</th>
<th>Participants</th>
<th>Intervention</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Batarfi A et al 2020</td>
<td>Multi-center cross-sectional study</td>
<td>Patients receiving oral anticoagulation (heart valve disease, rhythm disorder, vein thrombosis)</td>
<td>808 patients</td>
<td>Ramadan fasting</td>
</tr>
<tr>
<td>Kul S et al 2014</td>
<td>Meta-analysis of self-controlled cohort studies</td>
<td>Healthy population</td>
<td>1,476 patients</td>
<td>Ramadan fasting</td>
</tr>
<tr>
<td>Okoshi K et al 2019</td>
<td>Animal study</td>
<td>Wistar rats with induced myocardial infarction</td>
<td>N/A</td>
<td>Intermittent fasting (fed every other day)</td>
</tr>
</tbody>
</table>

Patient-guided modification of oral anticoagulation regime is common during Ramadan. Patients on twice daily anticoagulation are more likely to modify their treatment regime and are more likely to encounter bleeding or thromboembolic complications as a result. Patient education and, where possible, pre-Ramadan modification of treatment regimes may help avoid complications from patient non-compliance or uninformed adjustments.
<table>
<thead>
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<td>Ma X et al 2019</td>
<td>Animal study</td>
<td>Mice with induced proteotoxic cardiomyopathy</td>
<td>Intermittent fasting</td>
<td>In mice with induced advanced proteotoxic cardiomyopathy, intermittent fasting resulted in restored lysosomal abundance and autophagic flux. Left ventricular dilatation and myocardial hypertrophy was also attenuated, with mice demonstrating increased percentage fractional shortening and increased survival.</td>
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<td>Mousavi M et al 2014</td>
<td>Nonrandomised prospective observational study</td>
<td>Stable coronary artery disease with normal left ventricular function</td>
<td>Ramadan fasting</td>
<td>-Mean age of the cohort was 61.5 years. 50% were male -66% of patients completed Ramadan fast with an average of 22 days of fasting -Chest pain and shortness of breath occurrence was not significantly different between the fasting and non-fasting groups</td>
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<td>Prospective observational study</td>
<td>Patients with at least one cardiovascular risk factor (previous coronary artery disease, metabolic syndrome or cerebrovascular disease in the last 10 years)</td>
<td>Ramadan fasting</td>
<td>-A significant improvement in 10 years coronary heart disease risk (based on the Framingham risk score) was found in patients undergoing Ramadan fasting. -Patients undergoing Ramadan fasting had a significantly higher high-density lipoprotein and lower plasma cholesterol, triglyceride level, systolic blood pressure, body mass index and waist circumference (p&lt;0.05).</td>
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<td>Salam A et al 2017</td>
<td>Prospective multicentre study</td>
<td>Patients hospitalised with acute heart failure</td>
<td>Ramadan fasting</td>
<td>-306 (7.4%) patients were hospitalised with acute heart failure in the month of Ramadan in 2012. -3,851 (92.6%) patients were hospitalised with acute heart failure outside of Ramadan in the period of February to November 2012. This study represents (at the time of publication) the largest evaluation of the effects of fasting on acute heart failure. It reported an improved volume status in fasting patients. There were also</td>
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**Tempizhan A et al 1999**  
Retrospective review  
Acute coronary syndrome  
1,655 patients  
Ramadan fasting (indirect)  
The incidence of acute coronary syndrome in Ramadan in comparison to the remainder of the year in a geographically defined population  
6 years  
The incidence of acute coronary syndrome was significantly lower in Ramadan from 1991 to 1997 in a single centre in Turkey.  
The authors speculate that Ramadan fasting does not increase acute coronary syndrome.

| References |
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## Supplementary index

### Table 1: Summary of relevant studies cited in our paper

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<th>Study authors</th>
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<th>Cardiac condition</th>
<th>Number of patients</th>
<th>Type of fasting</th>
<th>Study objective</th>
<th>Follow up duration</th>
<th>Main findings</th>
<th>Conclusion</th>
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</table>
| Abazid et al 2018   | Prospective nonrandomised study           | HFrEF             | 249                | Ramadan fasting  | % of patients who became haemodynamically unstable and their clinical profile | 1 month (Ramadan) | -92% of patients remained haemodynamically stable  
-Profile of patients who became haemodynamically unstable:  
--higher initial NYHA class (2.19±0.9 vs. 1.6±0.8)  
--less adherence to medications (67% vs 94%)  
--less likely to have ischaemic cardiomyopathy (33% vs 57%) | "In most patients with chronic HFrEF, Ramadan fasting is considered safe. Non-adherence to medication and diet are significantly associated with decompensated heart failure during Ramadan" |
| Al Suwaidi et al 2005 | Retrospective review population-based study | HFrEF             | 20,856             | Ramadan fasting  | Whether Ramadan fasting has any effect on the number of hospitalisations for HFrEF in a geographically defined population | Records over a 10-year period were reviewed (January 1991 to December 2001) | -The number of hospitalisations for HFrEF was not significantly different in Ramadan (208 cases) when compared to a month before Ramadan (182 cases) and a month after Ramadan (198 cases) p>0.37.  
-There was no significant difference found in the baseline clinical characteristics or mortality (11.5%, 7.7% and 9.6%, respectively; p>0.43) in patients presenting in various time periods. | In this defined population, no significant difference was found in number of hospitalisations for HFrEF while fasting in Ramadan when compared to non-fasting months |
| Aslam M and Healy MA 1986 | Prospective review                          | Not specified. 3 out of 81 had cardiac conditions. | 81 Asian          | Ramadan fasting  | Medication compliance during Ramadan fasting                                    | 1 month (Ramadan) | -35 patients missed doses  
-8 patients took their tablets at different times  
-4 patients took all their medication as one single daily dose while breaking their fast in the evening | Medication noncompliance remains a significant problem with patients fasting in Ramadan |
| Babineaux SM et al 2015 | Multi-country, retrospective, observational study | Type 2 Diabetes Mellitus | 3777 patients 508 physicians | Ramadan fasting  | To describe the characteristics and management of patients with diabetes who chose to fast in Ramadan in 2010 | 73 months | -Oral antihyperglycemic therapy was the predominant pre-Ramadan therapy for most patients (76.6%)  
-Treatment regime was modified before Ramadan for 39.3% of all patients  
-Almost all physicians (96.2%) reported provided fasting-specific advice to patients  
-62.6% of physicians report using guidelines or recommendations for the management of diabetes during Ramadan | Physicians have increasingly adopted multiple approaches to the management of fasting during Ramadan, including the adoption of international and/or national guidelines, such that patients are able to fast for a greater number of days without acute complications. |
<table>
<thead>
<tr>
<th>Authors</th>
<th>Study Type</th>
<th>Population</th>
<th>Sample Size</th>
<th>Intervention</th>
<th>Duration</th>
<th>Findings</th>
</tr>
</thead>
</table>
| Batarfi A et al 2020 | Multi-center cross-sectional study | Patients receiving oral anticoagulation (heart valve disease, rhythm disorder, vein thrombosis) | 808 patients | Ramadan fasting | 3 months | -64% of patients reported fasting every day of Ramadan  
-20.2% of patients fasted for at least 15 days  
-68.4% of patients were taking warfarin, 31.6% were taking a direct oral anticoagulant  
-19.1% of patients were prescribed twice daily anticoagulation  
-During Ramadan, 46.9% of patients reported taking their anticoagulation as prescribed to them.  
-The remaining 53.1% of patients reported modifying drug intake in different ways (31.1% adjusting the time of intake, 13.2% skipped intakes and 2.2% double dosed).  
-Twice daily anticoagulation was a strong independent predictor for modification during Ramadan  
-The rate of hospital admission due to either bleeding or thromboembolic complications was higher in patients that modified treatment regimens (15.4%) as compared to adherent patients (6.6%). |
| Kul S et al 2014 | Meta-analysis of self-controlled cohort studies | Healthy population | 1,476 patients | Ramadan fasting | -64% of patients were taking warfarin, 31.6% were taking a direct oral anticoagulant  
-19.1% of patients were prescribed twice daily anticoagulation  
-During Ramadan, 46.9% of patients reported taking their anticoagulation as prescribed to them.  
-The remaining 53.1% of patients reported modifying drug intake in different ways (31.1% adjusting the time of intake, 13.2% skipped intakes and 2.2% double dosed).  
-Twice daily anticoagulation was a strong independent predictor for modification during Ramadan  
-The rate of hospital admission due to either bleeding or thromboembolic complications was higher in patients that modified treatment regimens (15.4%) as compared to adherent patients (6.6%). |
| Okoshi K et al 2019 | Animal study | Wistar rats with induced myocardial infarction | N/A | Intermittent fasting (fed every other day) | 3 months | -Final body weight and total mortality was lower in the intermittent fasting rats when compared to fasts fed every day.  
-At baseline, there was no difference in echocardiographic parameters.  
-12 weeks after MI was induced, intermittent fasting rats had a smaller posterior left ventricular wall thickness, reduced MI size, myocyte diameter and left ventricular volume.  
-Intermittent fasting initiated before or after MI reduces myocyte hypertrophy and LV dilatation.  
-Myocardial fibrosis and fetal gene expression are not modulated by feeding regimens.  
-Benefit is more evident when intermittent fasting is initiated before rather than after MI. |

Patient-guided modification of oral anticoagulation regime is common during Ramadan. Patients on twice daily anticoagulation are more likely to modify their treatment regime and are more likely to encounter bleeding or thromboembolic complications as a result. Patient education and, where possible, pre-Ramadan modification of treatment regimes may help avoid complications from patient non-compliance or uninformed adjustments.
Ma X et al 2019 | Animal study | Mice with induced proteotoxic cardiomyopathy | N/A | Intermittent fasting | To test whether TFEB (a master regulator of the autophagy-lysosomal pathway) activation in the myocardium can be harnessed to treat advanced proteotoxic cardiomyopathy | In mice with induced advanced proteotoxic cardiomyopathy, intermittent fasting resulted in restored lysosomal abundance and autophagic flux. Left ventricular dilatation and myocardial hypertrophy was also attenuated, with mice demonstrating increased percentage fractional shortening and increased survival. | Intermittent fasting and TFEB activation are clinically relevant therapeutic strategies to rescue advanced proteotoxic cardiomyopathy by normalising desmin localisation via autophagy-dependent and autophagy-independent mechanisms. |

Mousavi M et al 2014 | Nonrandomised prospective observational study | Stable coronary artery disease with normal left ventricular function | 148 patients | Ramadan fasting | To investigate the effects of Ramadan fasting in patients with coronary artery disease | Mean age of the cohort was 61.5 years. 50% were male. 66% of patients completed Ramadan fast with an average of 22 days of fasting. Chest pain and shortness of breath occurrence was not significantly different between the fasting and non-fasting groups. | Patients with coronary artery disease were able to observe the Ramadan fast safely and their combined endpoint of chest pain and dyspnoea was not significantly different from that of the non-fasting ones. The authors suggest that patients with stable coronary artery disease and normal left ventricular function could fast during Ramadan. |

Nematy M et al 2012 | Prospective observational study | Patients with at least one cardiovascular risk factor (previous coronary artery disease, metabolic syndrome or cerebrovascular disease in the last 10 years) | 82 patients | Ramadan fasting | The association of Ramadan fasting and cardiovascular risk factors | A significant improvement in 10 years coronary heart disease risk (based on the Framingham risk score) was found in patients undergoing Ramadan fasting. Patients undergoing Ramadan fasting had a significantly higher high-density lipoprotein and lower plasma cholesterol, triglyceride level, systolic blood pressure, body mass index and waist circumference (p<0.05). | A significant improvement in 10 years coronary heart disease risk score and other cardiovascular risk factors were noted after Ramadan fasting in patients with at least one cardiovascular risk factor. |

Salam A et al 2017 | Prospective multi-centre study | Patients hospitalised with acute heart failure | 4,157 patients | Ramadan fasting | The association of Ramadan fasting with outcomes in patients with | -306 (7.4%) patients were hospitalised with acute heart failure in the month of Ramadan in 2012. -3,851 (92.6%) patients were hospitalised with acute heart failure outside of Ramadan in the period of February to November 2012. | This study represents (at the time of publication) the largest evaluation of the effects of fasting on acute heart failure. It reported an improved volume status in fasting patients. There were also
Patients admitted with acute heart failure during Ramadan had significantly lower prevalence of symptoms and signs of volume overload compared to patients hospitalised in other months. Atrial arrhythmias were significantly less frequent and cholesterol levels were significantly lower in Ramadan. Hospitalisation in Ramadan was not independently associated with increased immediate or 1-year mortality. Favourable effects on atrial arrhythmias and total cholesterol and no effects on immediate or long-term outcomes.

<table>
<thead>
<tr>
<th>Study</th>
<th>Methodology</th>
<th>Syndrome</th>
<th>Ramadan fasting</th>
<th>Findings</th>
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<td>Turin T et al 2016</td>
<td>Systematic review and meta-analysis</td>
<td>Coronary heart disease Stroke Congestive heart failure</td>
<td>Ramadan fasting</td>
<td>To present a summary of key findings of all the published data on Ramadan fasting in patients with cardiovascular disease</td>
<td>The incidence of cardiovascular events during Ramadan was similar to those found in the remaining, non-fasting, months of the year. Ramadan fasting is not associated with any change in incidence of acute cardiovascular disease.</td>
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References


