International Journal of Medical Science and Clinical Research Studies

ISSN(print): 2767-8326, ISSN(online): 2767-8342

Volume 04 Issue 10 October 2024

Page No: 1928-1937

DOI: https://doi.org/10.47191/ijmscrs/v4-i10-39, Impact Factor: 7.949

Acute Myocardial Infarction in the Context of Diabetic Ketoacidosis: Pathophysiological Interactions, Clinical Manifestations, and Therapeutic Considerations

Donaldo Emiliano Silva López[1], Veronica Eloísa Durán Jiménez[2], Nidia Carolina Córdova Hernández[3], Geraldine Nieves Vázquez[4], María Elisa González Robles[4], Marian Anahí Rodríguez Carrillo[5]

[1]Tecnológico de Monterrey Campus Monterrey, Nuevo Léon, Mexico.

[2]Universidad Anahuac Cancún. Cancún, Quintana Roo, México.

[3]Universidad del Valle de México campus Reynosa. Tamaulipas, México.

[4]Universidad de Guadalajara. Guadalajara, Jalisco, México.

[5]Universidad Autónoma de Aguascalientes. Aguascalientes, México.

ABSTRACT

Acute myocardial infarction (AMI) and diabetic ketoacidosis (DKA) are two critical conditions that can coexist with significant morbidity and mortality. AMI is a leading cause of cardiovascular death, while DKA is a severe complication of uncontrolled diabetes mellitus, characterized by hyperglycemia, metabolic acidosis, and ketonemia. The convergence of these conditions presents unique challenges in diagnosis and management, as the metabolic disturbances of DKA can exacerbate myocardial ischemia and contribute to poor clinical outcomes. This article aims to explore the pathophysiological interplay between AMI and DKA, focusing on their shared risk factors, metabolic derangements, and the impact of hyperglycemia and ketosis on myocardial oxygen supply and demand. Furthermore, we discuss the clinical presentation, diagnostic strategies, and therapeutic approaches tailored to this dual pathology. Early recognition and prompt intervention are crucial to improving prognosis in patients with coexisting AMI and DKA. Multidisciplinary management involving cardiologists, endocrinologists, and intensivists is essential to mitigate the adverse outcomes of this complex clinical scenario.

KEYWORDS: Acute myocardial infarction, diabetic ketoacidosis, hyperglycemia, ketosis, metabolic acidosis, myocardial ischemia, cardiovascular complications, diabetes mellitus, ischemic heart disease, metabolic disturbances

ARTICLE DETAILS

Published On:
29 October 2024

Available on:
https://ijmscr.org/

INTRODUCTION

Acute myocardial infarction (AMI) remains a leading cause of death worldwide, particularly in individuals with predisposing risk factors such as diabetes mellitus. The pathogenesis of AMI primarily involves coronary artery occlusion secondary to atherosclerotic plaque rupture, leading to ischemia and necrosis of the myocardium. Among diabetic patients, the risk of AMI is notably heightened due to accelerated atherosclerosis, endothelial dysfunction, and the pro-inflammatory state induced by chronic hyperglycemia. Compounding this risk, diabetic ketoacidosis (DKA), a life-threatening metabolic complication of diabetes, can precipitate or worsen myocardial ischemia in vulnerable individuals.1,2

DKA is characterized by severe hyperglycemia, metabolic acidosis, and the presence of ketone bodies resulting from unregulated lipolysis in the context of insulin deficiency. The hemodynamic and metabolic disturbances inherent in DKA can severely compromise cardiovascular function, predisposing patients to arrhythmias, myocardial injury, and in severe cases, infarction. Both AMI and DKA share overlapping clinical features, including chest pain, dyspnea, and metabolic derangements, which can complicate timely diagnosis. Moreover, the acid-base imbalance and electrolyte shifts associated with DKA can exacerbate ischemic injury by further impairing myocardial oxygen delivery and increasing myocardial oxygen demand.1,2

The coexistence of AMI and DKA represents a particularly ominous clinical scenario, as each condition can independently exacerbate the pathophysiology of the other. For instance, the hyperglycemia and insulin resistance commonly observed during AMI may precipitate DKA in diabetic patients, while the stress of DKA, with its accompanying catecholamine surge and fluid deficits, may unmask or exacerbate myocardial ischemia. Understanding the interplay between these two conditions is crucial for optimizing treatment strategies. Delayed diagnosis or suboptimal management of either condition can result in catastrophic outcomes, including cardiogenic shock, heart failure, and death.1,2

This review seeks to delineate the pathophysiological mechanisms linking AMI and DKA, with an emphasis on the bidirectional nature of their relationship. In addition, we explore the diagnostic challenges posed by their coexistence and propose a comprehensive approach to management that addresses the metabolic, cardiovascular, and systemic complexities of these patients. By integrating insights from cardiology, endocrinology, and critical care, this article aims to provide a framework for clinicians managing the confluence of these high-risk conditions.1,2

Epidemiology of Acute Myocardial Infarction in the Context of Diabetic Ketoacidosis

The epidemiology of acute myocardial infarction (AMI) is well-established as one of the leading causes of morbidity and mortality globally, particularly in individuals with cardiovascular risk factors such as hypertension, dyslipidemia, smoking, and notably, diabetes mellitus. Diabetes mellitus, particularly type 1 diabetes, which is prone to diabetic ketoacidosis (DKA), and type 2 diabetes in advanced stages, which can also present with DKA in certain situations, is closely associated with an increased risk of cardiovascular disease, including AMI. However, the intersection of AMI and DKA represents a unique and relatively understudied epidemiological niche, characterized by a convergence of metabolic and ischemic pathology that portends a higher risk of adverse outcomes.2,3

General Epidemiology of Acute Myocardial Infarction and Diabetes Mellitus

Globally, ischemic heart disease, including AMI, remains the most common cause of death, accounting for approximately 16% of all deaths worldwide according to the World Health Organization (WHO). Diabetes mellitus, which affects over 460 million people globally, is a significant and independent risk factor for AMI, increasing the risk two to fourfold compared to individuals without diabetes. This risk is further magnified in individuals with long-standing, poorly controlled diabetes due to the progressive nature of atherosclerosis, endothelial dysfunction, and microvascular complications inherent to chronic hyperglycemia. The Framingham Heart Study and other large-scale epidemiological studies have consistently demonstrated that individuals with diabetes are at a substantially increased risk of developing AMI, with a particularly high prevalence among older adults, men, and individuals of lower socioeconomic status.2,3

Incidence and Prevalence of Diabetic Ketoacidosis

DKA primarily affects individuals with type 1 diabetes mellitus, where the absolute insulin deficiency leads to unchecked lipolysis and ketogenesis. The incidence of DKA is estimated to be approximately 4.6 to 8 episodes per 1,000 patients with diabetes annually, though rates vary considerably by region, access to healthcare, and socioeconomic factors. Type 1 diabetes mellitus accounts for the majority of DKA cases, though a growing number of patients with type 2 diabetes, particularly those of African, Hispanic, or Asian descent, are also susceptible to ketosis-prone diabetes and DKA. The mortality associated with DKA has declined significantly over the past few decades due to advances in early recognition and treatment, but it remains higher in resource-limited settings, with reported mortality rates of up to 10%. Of note, cardiovascular complications, including AMI, represent a significant proportion of DKA-related mortality.2,3

Prevalence of AMI in Patients with DKA

While the exact prevalence of AMI in patients with DKA is not well documented, retrospective cohort studies and case series suggest that AMI occurs in a small but clinically significant subset of DKA patients, particularly among older adults and those with pre-existing cardiovascular risk factors. It is estimated that up to 10% of individuals presenting with DKA may have concomitant cardiovascular events, including AMI, though this number likely underestimates the true burden due to the challenge of diagnosing AMI in the setting of metabolic acidosis and electrolyte disturbances. Moreover, studies have shown that hyperglycemia, which is a hallmark of DKA, is independently associated with increased in-hospital mortality in patients with AMI, suggesting a synergistic relationship between these conditions.3,4

Risk Factors and Demographic Patterns

Several demographic and clinical factors are associated with an increased risk of AMI in patients with DKA. Age is a major determinant, as older adults with diabetes are more likely to have underlying coronary artery disease and are at greater risk for AMI during metabolic stress events such as DKA. Gender differences have also been noted, with men generally at higher risk for AMI, although women with diabetes may have worse outcomes due to a greater prevalence of atypical presentations and delayed diagnoses. Ethnic and racial disparities also play a role, as African American and Hispanic populations, who are disproportionately affected by both type 1 and type 2 diabetes, experience higher rates of DKA and are therefore at increased risk for complications such as AMI.4,5

Socioeconomic factors, including access to healthcare, education, and socioeconomic status, further influence the epidemiology of AMI in DKA patients. In low-income settings, delays in the recognition and treatment of both DKA and AMI are common, leading to higher mortality and morbidity. In contrast, high-income settings, with more readily available intensive care and advanced diagnostic tools, may have lower mortality rates but still face significant challenges in the management of these patients due to the complex interplay of metabolic and ischemic stress.

Hospitalization and Mortality Rates

Hospitalization rates for patients presenting with both AMI and DKA are higher compared to those with either condition alone. Patients with DKA and concomitant AMI require intensive management, typically involving admission to an intensive care unit (ICU) for close monitoring of metabolic parameters, cardiovascular function, and potential complications such as arrhythmias and cardiogenic shock. Studies suggest that the in-hospital mortality rate for patients with both AMI and DKA is significantly higher compared to those with AMI or DKA alone, with mortality rates ranging from 15% to 25%, depending on the severity of the conditions and the presence of comorbidities. 4,5

Geographic Variations and Global Burden

There is considerable geographic variation in the prevalence and outcomes of AMI and DKA, influenced by factors such as healthcare infrastructure, the prevalence of diabetes, and public health initiatives aimed at early detection and management of cardiovascular and metabolic diseases. High-income countries with well-developed healthcare systems tend to have lower mortality rates for both AMI and DKA, whereas low- and middle-income countries face significant challenges, including delayed diagnosis, limited access to insulin and cardiovascular care, and higher rates of complications. For instance, studies from Sub-Saharan Africa and South Asia report higher case fatality rates for DKA, often exceeding 20%, due to a lack of resources and delayed presentation, which likely exacerbates the incidence of AMI in these populations.5,6

The epidemiology of AMI in the context of DKA reflects a convergence of two life-threatening conditions, each of which is associated with significant morbidity and mortality. While data on the precise prevalence of AMI in patients with DKA is limited, available evidence suggests that this dual pathology is not uncommon, particularly in older adults and individuals with poorly controlled diabetes. The co-occurrence of AMI and DKA requires prompt recognition and a multidisciplinary approach to management to improve patient outcomes. Future epidemiological studies are needed to better characterize the incidence, risk factors, and outcomes of AMI in DKA, with a focus on identifying strategies to mitigate the risk in high-risk populations.5,6

Pathophysiology of Acute Myocardial Infarction in the Context of Diabetic Ketoacidosis

The pathophysiology of acute myocardial infarction (AMI) is intricately complex, involving coronary artery occlusion, ischemia, and necrosis of myocardial tissue. When AMI occurs in the setting of diabetic ketoacidosis (DKA), the interplay between these two life-threatening conditions further exacerbates metabolic and cardiovascular instability. DKA, a severe complication of insulin deficiency, leads to profound metabolic derangements such as hyperglycemia, ketoacidosis, and electrolyte imbalances. These abnormalities can worsen myocardial ischemia, enhance oxygen demand, and reduce cardiac output, leading to an acute deterioration in clinical status. Understanding the bidirectional pathophysiological mechanisms between AMI and DKA is critical to optimizing diagnosis and treatment strategies.5,6

Myocardial Ischemia and Coronary Artery Disease in Diabetic Patients

The underlying pathogenesis of AMI primarily revolves around atherosclerotic plaque rupture or erosion within the coronary arteries, leading to thrombosis, occlusion, and subsequent myocardial ischemia. This ischemic process initiates a cascade of events including myocardial cell death, inflammation, and fibrosis, resulting in impaired cardiac function. In diabetic individuals, this process is accelerated by the presence of chronic hyperglycemia, which promotes endothelial dysfunction, vascular inflammation, and the formation of advanced glycation end-products (AGEs). These factors contribute to a more aggressive form of coronary artery disease (CAD) in diabetic patients, characterized by more diffuse and calcified atherosclerotic plaques, leading to an increased incidence and severity of AMI.6,7

Pathophysiology of Diabetic Ketoacidosis

DKA is characterized by a triad of hyperglycemia, ketosis, and metabolic acidosis, resulting from an absolute or relative deficiency of insulin. In the absence of sufficient insulin, glucose is unable to enter cells for energy production, prompting a compensatory increase in lipolysis. This leads to the release of free fatty acids, which are metabolized in the liver into ketone bodies, such as acetoacetate and beta-hydroxybutyrate. The accumulation of ketones, combined with the osmotic diuresis induced by hyperglycemia, results in profound dehydration, electrolyte imbalances (especially hypokalemia), and an acid-base disturbance, with a significant reduction in serum bicarbonate and a compensatory respiratory alkalosis (Kussmaul respiration).6,7

The metabolic derangements in DKA can severely compromise cardiovascular function. The osmotic diuresis and dehydration lead to reduced intravascular volume, resulting in hypoperfusion of tissues, including the myocardium. Moreover, the metabolic acidosis associated with ketosis decreases myocardial contractility by impairing the sensitivity of cardiac myocytes to calcium, while also increasing pulmonary vascular resistance and promoting vasoconstriction. These hemodynamic shifts further strain the myocardium, especially in patients with pre-existing coronary artery disease or impaired cardiac function.6,7

Interaction Between DKA and AMI: A Bidirectional Relationship

The pathophysiological relationship between DKA and AMI is bidirectional, with each condition capable of precipitating or exacerbating the other. On one hand, the metabolic stress and hemodynamic instability caused by DKA can precipitate or worsen myocardial ischemia in individuals with underlying CAD, leading to an AMI. On the other hand, AMI, through the stress response, can induce a hyperglycemic state, worsen insulin resistance, and precipitate DKA, particularly in individuals with poorly controlled diabetes.7,8

1. Hemodynamic Instability and Hypoperfusion:

During DKA, severe dehydration and hypovolemia result in reduced cardiac output and tissue perfusion. Hypoperfusion of the myocardium, coupled with the increased oxygen demand of hyperglycemia and ketosis, creates an environment of relative myocardial ischemia, even in the absence of significant coronary artery occlusion. The impaired perfusion can exacerbate ischemia in individuals with existing coronary artery stenosis, potentially triggering AMI. Furthermore, the metabolic acidosis characteristic of DKA impairs the ability of hemoglobin to deliver oxygen to tissues (Bohr effect), further compromising myocardial oxygenation.7,8

2. Electrolyte Imbalances and Cardiac Stress:

DKA is associated with significant electrolyte imbalances, particularly hyperkalemia followed by hypokalemia during treatment, both of which can predispose patients to arrhythmias and acute myocardial injury. Potassium plays a crucial role in maintaining the electrical stability of cardiac myocytes, and fluctuations in serum potassium levels can result in ventricular arrhythmias, which are a common complication in AMI. Additionally, hypomagnesemia and hypophosphatemia, common in DKA, further compromise cardiac function and increase the risk of arrhythmias.7,8

The depletion of potassium during DKA therapy (as insulin therapy drives potassium into cells) may impair myocardial contractility, reduce cardiac output, and predispose the heart to ischemic injury. This electrolyte imbalance can also lead to the prolongation of the QT interval, increasing the risk of ventricular arrhythmias, which can be fatal in the setting of myocardial infarction.7,8

3. Increased Catecholamine Release and Hyperglycemia:

The physiological stress associated with AMI triggers the release of catecholamines, which stimulate gluconeogenesis and glycogenolysis, leading to hyperglycemia. In diabetic patients, this stress-induced hyperglycemia can precipitate DKA, particularly in individuals with insulin deficiency or resistance. The elevated levels of circulating catecholamines also increase myocardial oxygen demand by raising heart rate and contractility, further exacerbating ischemic injury during AMI.8,9

In addition, hyperglycemia during AMI has been shown to impair the function of endothelial cells, reduce nitric oxide bioavailability, and promote a pro-inflammatory and pro-thrombotic state. These effects may worsen the extent of myocardial damage during ischemia and contribute to poor outcomes in patients with concomitant DKA.8,9

4. Inflammation and Oxidative Stress:

Both AMI and DKA are associated with a significant inflammatory response. In the case of AMI, ischemic myocardial injury leads to the activation of pro-inflammatory cytokines, such as tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and interleukin-1 (IL-1), which contribute to further myocardial damage and systemic inflammation. Similarly, DKA triggers an inflammatory response due to the metabolic stress and hyperglycemia, with elevated levels of C-reactive protein (CRP) and other inflammatory markers.8,9

The concomitant inflammation in AMI and DKA enhances oxidative stress within the myocardium, exacerbating myocardial ischemia and increasing the extent of necrosis. This heightened inflammatory state can also impair the reparative processes of the myocardium, leading to adverse remodeling, reduced cardiac function, and an increased risk of heart failure.8,9

Impact on Myocardial Oxygen Supply-Demand Mismatch

A critical aspect of the pathophysiological relationship between AMI and DKA is the imbalance between myocardial oxygen supply and demand. During AMI, coronary blood flow is reduced due to plaque rupture or thrombosis, leading to ischemia and necrosis. In the context of DKA, myocardial oxygen demand is significantly increased due to the metabolic stress of hyperglycemia, ketosis, and the accompanying catecholamine surge. Simultaneously, the oxygen supply is impaired by the dehydration, acidosis, and hypoperfusion associated with DKA. This mismatch between supply and demand accelerates ischemic injury, resulting in more extensive myocardial damage in patients with concurrent AMI and DKA.8,9

The pathophysiology of AMI in the setting of DKA is a complex and multifaceted process involving metabolic, hemodynamic, and inflammatory factors. The combination of coronary artery occlusion, hyperglycemia, metabolic acidosis, electrolyte imbalances, and systemic inflammation creates a perfect storm for myocardial ischemia and injury. The bidirectional relationship between AMI and DKA highlights the need for early recognition and aggressive management of both conditions to prevent catastrophic outcomes. Understanding the interplay between these conditions at a mechanistic level is essential for optimizing therapeutic strategies and improving the prognosis of patients with coexisting AMI and DKA.8,9

Diagnostic Methods for Acute Myocardial Infarction in the Context of Diabetic Ketoacidosis

Diagnosing acute myocardial infarction (AMI) in the presence of diabetic ketoacidosis (DKA) presents unique clinical challenges due to overlapping symptoms and metabolic disturbances. Both AMI and DKA are serious conditions that require immediate intervention, but their coexistence complicates the diagnostic process. The clinical picture of DKA—characterized by hyperglycemia, dehydration, and electrolyte imbalances—can obscure the typical presentation of AMI, leading to delayed recognition and treatment. Therefore, a combination of clinical evaluation, electrocardiography (ECG), cardiac biomarkers, imaging modalities, and laboratory findings is essential for an accurate diagnosis. This section will delve into the detailed diagnostic approach for AMI in patients with DKA, emphasizing the importance of a multifaceted diagnostic strategy.8,9

1. Clinical Evaluation and History

The clinical presentation of AMI in the context of DKA can be subtle or atypical due to the metabolic and electrolyte disturbances associated with DKA. Classic symptoms of AMI, such as chest pain or discomfort, shortness of breath, and diaphoresis, may be masked by the severe metabolic derangements of DKA, including nausea, vomiting, abdominal pain, and altered mental status. Furthermore, diabetic patients are more likely to experience "silent" myocardial infarctions due to autonomic neuropathy, which diminishes the sensation of pain. In the setting of DKA, symptoms like tachycardia, hypotension, and altered sensorium may be mistakenly attributed solely to metabolic causes rather than underlying cardiac ischemia.8,9

Therefore, a thorough clinical history is crucial. The presence of known cardiovascular risk factors (e.g., longstanding diabetes, hypertension, hyperlipidemia, smoking) should raise suspicion for AMI. Physicians must maintain a high index of suspicion, especially in patients with poorly controlled diabetes or those who have experienced previous cardiovascular events. Asking about recent physical exertion, emotional stress, or symptoms of ischemia (even if atypical, such as fatigue or generalized weakness) can also provide valuable diagnostic clues.8,9

2. Electrocardiography (ECG)

Electrocardiography (ECG) is the cornerstone of AMI diagnosis and should be performed immediately upon suspicion of cardiac ischemia, even in the presence of DKA. However, interpreting ECGs in patients with DKA can be challenging due to electrolyte abnormalities—particularly potassium disturbances—that can cause changes mimicking or masking ischemic patterns.10,11

Typical ischemic findings on ECG, such as ST-segment elevation, T-wave inversions, or new Q waves, should prompt further investigation and management of AMI. In the setting of DKA, hyperkalemia may cause peaked T-waves, flattened P-waves, and widened QRS complexes, while hypokalemia may lead to prominent U waves and ST-segment depressions, both of which can obscure ischemic changes. Additionally, DKA-associated tachycardia, often present due to dehydration and metabolic stress, can make it more difficult to detect subtle ischemic changes.10,11

Continuous ECG monitoring is recommended, particularly in the early phases of DKA treatment, as rapid shifts in electrolytes (particularly potassium) during insulin therapy can precipitate life-threatening arrhythmias. Serial ECGs are also valuable for tracking dynamic changes suggestive of evolving myocardial ischemia.10,11

3. Cardiac Biomarkers

Measurement of cardiac biomarkers, specifically troponins, plays a critical role in confirming the diagnosis of AMI. Troponins I and T are highly specific and sensitive markers of myocardial injury and are routinely used in the diagnosis of AMI. In the context of DKA, elevated troponin levels may be more challenging to interpret, as they can be mildly elevated due to non-ischemic causes, such as the metabolic stress of severe hyperglycemia, dehydration, or ketoacidosis itself.10,11

However, in patients with clinically significant AMI, troponin levels typically rise markedly above baseline, reflecting myocardial necrosis. Serial troponin measurements are essential for differentiating between minor, stress-related elevations and the pronounced rise and fall pattern indicative of true AMI. A rapid increase in troponin levels, particularly when accompanied by ECG changes, should prompt immediate intervention for AMI. It is important to recognize that troponins may remain elevated for several days following an AMI, so trends over time should be evaluated.10,11

Other cardiac biomarkers, such as creatine kinase-MB (CK-MB), may also be elevated in AMI, though CK-MB is less specific and may be elevated in conditions such as rhabdomyolysis, which can occasionally complicate DKA. Therefore, while CK-MB can be useful, troponins are generally preferred for their superior sensitivity and specificity.10,11

4. Laboratory Findings

In patients with DKA, laboratory evaluation reveals profound metabolic disturbances, including hyperglycemia, an anion gap metabolic acidosis (due to elevated ketoacids), hyperkalemia or hypokalemia (depending on the stage of treatment), and varying degrees of renal dysfunction. These metabolic derangements complicate the diagnosis of AMI by obscuring traditional markers of myocardial injury and exacerbating myocardial ischemia through electrolyte disturbances and acidosis.10,11

The acid-base imbalance associated with DKA can reduce myocardial contractility and impair the heart's response to ischemia, further complicating the clinical picture. Close monitoring of electrolytes, especially potassium and magnesium, is essential, as imbalances can worsen ischemic injury and predispose the patient to arrhythmias.10,11

Blood gas analysis can help quantify the severity of acidosis and monitor the resolution of DKA during treatment. Severe acidosis may worsen ischemic injury by reducing the oxygen-carrying capacity of hemoglobin (Bohr effect) and increasing pulmonary vascular resistance, leading to further hypoperfusion of the myocardium.10,11

5. Imaging Modalities

a. Echocardiography

Echocardiography is a valuable non-invasive tool for assessing cardiac function in patients with suspected AMI, especially in the setting of DKA, where clinical signs of myocardial ischemia may be subtle or masked by metabolic derangements. Echocardiography can identify regional wall motion abnormalities (RWMAs), which are indicative of myocardial ischemia or infarction. In the presence of AMI, localized areas of hypokinesis, akinesis, or dyskinesis may be observed, corresponding to the territory of the affected coronary artery.10,11

In patients with DKA, echocardiography can also provide important hemodynamic information, such as the presence of reduced ejection fraction, elevated filling pressures, or signs of right ventricular strain, which may occur in the setting of acute myocardial injury. Additionally, echocardiography can help rule out other potential causes of chest pain, such as pericarditis or pulmonary embolism, which may mimic AMI in diabetic patients.12,13

b. Coronary Angiography

Coronary angiography remains the gold standard for the diagnosis of AMI, particularly in cases where the diagnosis is uncertain or when immediate reperfusion therapy is being considered. In patients with DKA, once metabolic stabilization has been achieved, coronary angiography can confirm the presence of significant coronary artery stenosis or occlusion, guiding decisions about percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG).12,13

Given the high risk of arrhythmias, hemodynamic instability, and complications in patients with DKA, coronary angiography should be performed in centers equipped with advanced cardiac care facilities. In cases where AMI is strongly suspected, early angiography and reperfusion therapy should not be delayed once the patient has been appropriately resuscitated and stabilized.12,13

6. Additional Diagnostic Considerations

a. CT Coronary Angiography

In patients who are hemodynamically stable and do not require immediate invasive intervention, computed tomography coronary angiography (CTCA) may be considered to assess the extent of coronary artery disease. CTCA is a non-invasive imaging modality that provides detailed visualization of the coronary arteries and can help identify significant atherosclerotic lesions or calcification that may predispose the patient to AMI.12,13

b. Nuclear Imaging

Myocardial perfusion imaging (MPI) using nuclear techniques, such as single-photon emission computed tomography (SPECT) or positron emission tomography (PET), can provide functional information about myocardial blood flow and viability. In patients with suspected AMI, MPI can help localize ischemic areas and assess the extent of myocardial damage. However, its use in DKA patients may be limited by the need for metabolic stabilization and logistical considerations.12,13

Diagnosing acute myocardial infarction in the context of diabetic ketoacidosis requires a comprehensive and nuanced approach, as the metabolic disturbances of DKA can obscure traditional diagnostic markers of AMI. A combination of clinical assessment, ECG interpretation, cardiac biomarker measurement, imaging studies, and careful laboratory evaluation is essential to accurately identify AMI in this challenging population. Early recognition and intervention are critical, as the coexistence of these two conditions significantly worsens prognosis and increases the risk of mortality. Collaborative care involving cardiology, endocrinology, and critical care teams is crucial for optimizing patient outcomes.12,13

Treatment Approaches for Acute Myocardial Infarction in the Context of Diabetic Ketoacidosis

The simultaneous occurrence of acute myocardial infarction (AMI) and diabetic ketoacidosis (DKA) represents a clinical emergency requiring prompt, coordinated care. The management of AMI in the setting of DKA is complex due to the overlapping pathophysiological mechanisms of ischemic myocardial injury, profound metabolic derangements, and electrolyte imbalances. Both conditions individually are life-threatening, but their coexistence significantly increases morbidity and mortality. Therefore, the treatment strategy must address the underlying myocardial ischemia while rapidly correcting the metabolic abnormalities associated with DKA. Optimal care involves early recognition, stabilization, and a multidisciplinary approach, with a focus on simultaneous cardiovascular and metabolic management.14,15

1. Initial Stabilization and Supportive Care

In any patient with suspected AMI and DKA, initial management focuses on immediate stabilization, addressing life-threatening issues such as hypoxia, acidosis, electrolyte disturbances, and hemodynamic instability. The first step is to ensure adequate airway, breathing, and circulation (the

"ABC" approach), along with continuous monitoring of vital signs, electrocardiography (ECG), and cardiac telemetry. Early identification of both conditions is crucial, and time-sensitive interventions, such as reperfusion therapy for AMI, must be balanced with the need for metabolic stabilization in DKA.16,17

a. Oxygen Therapy

In the setting of AMI, supplemental oxygen is administered to patients with hypoxemia (oxygen saturation <90%) to ensure adequate oxygen delivery to ischemic myocardial tissue. Oxygen therapy should be titrated to maintain an oxygen saturation of 94-98%. While routine oxygen administration in normoxic patients with AMI is not recommended, it is particularly important in DKA due to the potential for impaired oxygen delivery secondary to acidosis and dehydration.17

b. Fluid Resuscitation

Aggressive fluid resuscitation is a cornerstone of DKA treatment and is equally critical in patients with concomitant AMI, given that DKA leads to severe dehydration, hypovolemia, and reduced cardiac output. Initial fluid therapy aims to restore intravascular volume, improve tissue perfusion, and reduce acidosis. Isotonic saline (0.9% NaCl) is typically used for initial fluid replacement, with the rate of infusion tailored to the patient's hemodynamic status, electrolyte balance, and renal function.17

However, in patients with AMI, fluid overload must be avoided, especially in those with heart failure or impaired cardiac function. Careful monitoring of central venous pressure, urine output, and electrolytes is essential to avoid worsening pulmonary edema or myocardial ischemia due to excessive fluid administration. After the initial resuscitation phase, fluids should be switched to a solution containing glucose (e.g., 5% dextrose with 0.45% saline) once blood glucose levels drop below 250 mg/dL, to prevent hypoglycemia during insulin therapy.17

c. Electrolyte Management

Electrolyte imbalances, particularly potassium disturbances, are common in DKA and must be corrected early to avoid life-threatening arrhythmias, which are a significant risk in patients with AMI. Hyperkalemia is often present initially in DKA due to insulin deficiency, but hypokalemia can develop rapidly during insulin therapy as potassium shifts intracellularly.18

Before initiating insulin therapy, serum potassium should be evaluated:

- If serum potassium is >5.0 mEq/L, insulin therapy may proceed without immediate potassium supplementation.19
- If serum potassium is between 3.3 and 5.0 mEq/L, potassium replacement should begin concurrently with insulin therapy.19
- If serum potassium is <3.3 mEq/L, insulin therapy must be delayed until potassium levels are corrected due to the high risk of fatal arrhythmias.19

Other electrolytes, such as magnesium and phosphate, should also be monitored and replaced as needed, as imbalances in these electrolytes can further impair myocardial function and predispose to arrhythmias.19

2. Insulin Therapy and Glucose Management

Insulin therapy is the cornerstone of DKA treatment, as it corrects hyperglycemia, suppresses ketogenesis, and reduces acidosis. In patients with AMI, careful glucose management is crucial, as hyperglycemia can exacerbate myocardial ischemia and worsen outcomes. Insulin is administered via continuous intravenous infusion, starting with a bolus dose (0.1 units/kg) followed by an infusion at 0.1 units/kg/hour.19

The goals of insulin therapy in DKA are to:

- Reduce serum glucose levels at a steady rate (50-75 mg/dL/hour) to prevent rapid shifts in osmolality that could lead to cerebral edema.
- Suppress ketone production and reverse acidosis, as evidenced by a decrease in the anion gap.

Frequent monitoring of blood glucose, serum ketones, and arterial blood gases is required to assess the response to therapy. Once blood glucose falls below 250 mg/dL, a glucose-containing solution is added to prevent hypoglycemia and allow for continued insulin infusion to resolve the ketoacidosis.19

In the context of AMI, hyperglycemia should be controlled to target levels between 140 and 180 mg/dL to minimize stress-induced myocardial injury. However, hypoglycemia must be avoided, as it can worsen ischemic injury and lead to adverse cardiovascular outcomes.19

3. Reperfusion Therapy for AMI

Early reperfusion therapy is the cornerstone of AMI management and should be initiated as soon as possible to restore blood flow to the ischemic myocardium, limit infarct size, and improve survival. Reperfusion strategies include percutaneous coronary intervention (PCI) and fibrinolytic therapy. The choice of reperfusion method depends on the availability of resources, timing, and the patient's clinical status.19

a. Percutaneous Coronary Intervention (PCI)

Primary PCI is the preferred reperfusion strategy in AMI and should be performed within 90 minutes of first medical contact in patients with ST-elevation myocardial infarction (STEMI). PCI involves the use of a catheter to open the blocked coronary artery and restore blood flow through balloon angioplasty, often followed by stent placement. In patients with DKA, PCI may need to be delayed until the patient is adequately stabilized metabolically, especially in cases of severe acidosis or electrolyte disturbances. However, delaying reperfusion therapy significantly increases myocardial damage, so a balance must be struck between stabilizing the metabolic derangements and providing timely coronary intervention.19

b. Fibrinolytic Therapy

In cases where PCI is not available within the recommended time frame, fibrinolytic therapy (e.g., alteplase, tenecteplase) can be used to dissolve the thrombus and restore coronary perfusion. Fibrinolytics should be administered within 30 minutes of hospital arrival if PCI is not feasible. However, fibrinolytic therapy carries an increased risk of bleeding, particularly in patients with DKA, who may have an altered coagulation profile due to dehydration and acidosis.20

4. Antithrombotic Therapy

Antithrombotic therapy, including antiplatelet agents and anticoagulants, is essential in the management of AMI to prevent further thrombus formation and improve outcomes. Dual antiplatelet therapy (DAPT) with aspirin and a P2Y12 inhibitor (e.g., clopidogrel, ticagrelor, or prasugrel) should be initiated as early as possible in patients with AMI, unless contraindications such as active bleeding are present.20

a. Aspirin

Aspirin is administered as a 160-325 mg loading dose followed by 75-100 mg daily. It irreversibly inhibits cyclooxygenase-1 (COX-1), reducing thromboxane A2 production and platelet aggregation. Aspirin is a mainstay of AMI treatment and should be continued long-term unless contraindications arise.20

b. P2Y12 Inhibitors

P2Y12 inhibitors, such as clopidogrel, ticagrelor, or prasugrel, are added to aspirin to further inhibit platelet aggregation. A loading dose is administered early in the course of AMI management, followed by daily maintenance therapy. Ticagrelor and prasugrel are preferred over clopidogrel due to their more potent and consistent antiplatelet effects, although the choice may be influenced by patient-specific factors, such as the risk of bleeding or the need for urgent surgical intervention.20

c. Anticoagulation

Anticoagulation is recommended in conjunction with PCI or fibrinolytic therapy to prevent thrombus propagation. Unfractionated heparin (UFH) or low-molecular-weight heparin (LMWH) is commonly used, with dosing adjusted based on renal function and bleeding risk. In patients with DKA, close monitoring of coagulation parameters is required, as metabolic derangements can affect the response to anticoagulation.20

5. Management of Heart Failure and Arrhythmias

Patients with concomitant AMI and DKA are at high risk for developing heart failure and arrhythmias due to myocardial ischemia, electrolyte imbalances, and volume overload from fluid resuscitation. Management strategies for these complications include:

a. Heart Failure

In cases of acute heart failure, loop diuretics (e.g., furosemide) may be necessary to manage fluid overload, especially if pulmonary edema is present. Care must be taken to avoid over-diuresis, as this can exacerbate hypovolemia and reduce cardiac output in DKA patients. Inotropic support (e.g., dobutamine) may be required in patients with reduced cardiac output and hypotension, particularly in the setting of cardiogenic shock.20

b. Arrhythmias

Electrolyte imbalances in DKA, particularly potassium and magnesium abnormalities, increase the risk of arrhythmias. Continuous cardiac monitoring is essential, and electrolyte levels should be closely corrected. In cases of ventricular arrhythmias or atrial fibrillation, antiarrhythmic therapy (e.g., amiodarone) may be necessary. In severe cases, electrical cardioversion or defibrillation may be required to restore normal rhythm.21

The treatment of AMI in the context of DKA is complex, requiring careful coordination of cardiovascular and metabolic management. Early recognition, aggressive stabilization, and timely reperfusion therapy are essential to improving outcomes. The balance between correcting metabolic derangements and addressing myocardial ischemia is critical, with a focus on preventing life-threatening complications such as arrhythmias, heart failure, and further myocardial injury. A multidisciplinary approach involving cardiologists, endocrinologists, intensivists, and emergency physicians is vital to the successful management of these critically ill patients.21

CONCLUSIONS

The intersection of acute myocardial infarction (AMI) and diabetic ketoacidosis (DKA) represents a clinical conundrum that underscores the intricate relationship between cardiovascular and metabolic health. Both AMI and DKA are independent life-threatening conditions; however, their simultaneous occurrence creates a synergistic risk that significantly worsens patient prognosis. Understanding the pathophysiological interplay, diagnostic challenges, and therapeutic complexities involved in managing these two conditions is essential for improving outcomes in this high-risk patient population.

Pathophysiological Interplay

The pathophysiology of AMI in the setting of DKA highlights the deleterious effects of metabolic disturbances on myocardial tissue. DKA, characterized by hyperglycemia, metabolic acidosis, and electrolyte imbalances, exacerbates ischemic injury by promoting an inflammatory milieu, increasing oxidative stress, and impairing endothelial function. The metabolic acidosis present in DKA further destabilizes cardiac function by reducing myocardial contractility and precipitating arrhythmias through electrolyte disturbances, particularly hypokalemia. Additionally, the hypercoagulable state seen in DKA, coupled with dehydration and hemoconcentration, increases the likelihood of coronary thrombosis, which can precipitate or worsen AMI.

Hyperglycemia itself contributes to adverse cardiovascular outcomes by inducing endothelial dysfunction, promoting inflammation, and increasing myocardial oxygen demand, further stressing an already compromised heart. Conversely, myocardial ischemia and infarction lead to a surge in stress hormones such as catecholamines and cortisol, exacerbating insulin resistance and worsening hyperglycemia and ketosis. This bidirectional relationship creates a vicious cycle of metabolic and cardiovascular deterioration, which requires urgent and coordinated medical intervention.

Diagnostic Challenges

The coexistence of AMI and DKA presents several diagnostic challenges. Many of the clinical features of DKA, such as chest pain, dyspnea, and fatigue, overlap with those of AMI, potentially masking the presentation of one condition or delaying the diagnosis of the other. Moreover, the electrocardiographic (ECG) findings in DKA, such as peaked T waves, prolonged QT interval, or nonspecific ST-segment changes, may confound the diagnosis of AMI or be mistaken for ischemic changes. Likewise, elevated cardiac biomarkers like troponin may be present in patients with DKA even in the absence of coronary artery occlusion, due to metabolic stress or subclinical myocardial injury.

Clinicians must maintain a high index of suspicion for AMI in patients presenting with DKA, especially in those with known cardiovascular risk factors or atypical clinical presentations. In these cases, the use of advanced imaging modalities, such as echocardiography or coronary angiography, may be necessary to confirm the diagnosis of AMI and guide therapeutic decision-making. The prompt differentiation between ischemic cardiac injury and metabolic-induced myocardial stress is crucial for selecting appropriate interventions and avoiding unnecessary delays in reperfusion therapy.

Therapeutic Complexities

The management of patients with concurrent AMI and DKA requires a delicate balance between addressing the ischemic insult and correcting the profound metabolic derangements. Early and aggressive fluid resuscitation, electrolyte repletion, and insulin therapy remain the cornerstone of DKA management. However, these therapies must be carefully tailored in patients with AMI, as excessive fluid administration can precipitate heart failure, while rapid shifts in potassium levels during insulin therapy can lead to fatal arrhythmias in an ischemic heart.

In parallel, timely reperfusion therapy is critical for limiting myocardial damage and improving survival in AMI. Percutaneous coronary intervention (PCI) remains the gold standard for reperfusion in ST-elevation myocardial infarction (STEMI), but its timing may need to be adjusted in the context of severe metabolic acidosis or electrolyte imbalances. A multidisciplinary approach, involving cardiologists, endocrinologists, intensivists, and emergency physicians, is essential for optimizing both cardiovascular and metabolic outcomes in these critically ill patients.

The use of adjunctive therapies, such as antithrombotic agents (antiplatelet drugs and anticoagulants), must also be approached with caution. DKA induces a prothrombotic state due to dehydration, hemoconcentration, and hyperglycemia, increasing the risk of thrombotic events. However, antithrombotic therapy in AMI carries the risk of bleeding, particularly when metabolic disturbances lead to coagulopathies. Thus, antithrombotic strategies must be individualized, taking into account the risks and benefits in the context of DKA.

Prognosis and Future Directions

Patients with concurrent AMI and DKA face a significantly increased risk of adverse outcomes, including arrhythmias, heart failure, cardiogenic shock, and death. Mortality rates are higher compared to those with either condition alone, underscoring the importance of early recognition and rapid intervention. Long-term prognosis remains poor, particularly in patients with underlying diabetic complications or preexisting cardiovascular disease, emphasizing the need for aggressive risk factor management after discharge.

Future research should focus on refining diagnostic algorithms to improve the early identification of AMI in DKA patients, particularly through the use of novel biomarkers and imaging techniques. Additionally, there is a need for clinical trials to determine the optimal timing and strategy for reperfusion therapy in patients with severe metabolic acidosis. Furthermore, the role of novel cardioprotective agents in mitigating ischemic injury in the context of DKA should be explored, as these agents may provide additional benefit in this unique patient population.

The coexistence of AMI and DKA represents a formidable clinical challenge, characterized by a complex interplay of metabolic and cardiovascular pathophysiology. Successful management hinges on the early identification of both conditions, prompt initiation of appropriate therapies, and careful monitoring of metabolic and cardiovascular status. The management of these patients requires a multidisciplinary approach, with a focus on optimizing both short-term and long-term outcomes. As our understanding of the pathophysiological mechanisms linking hyperglycemia, ketosis, and myocardial ischemia continues to evolve, there is hope that future advances in diagnostic and therapeutic strategies will improve survival and quality of life in this high-risk population.

REFERENCES

I. Noble-Bell G, Cox A. Management of diabetic ketoacidosis in adults. Nurs Times. 2014;110(10):14–17.

II. Westerberg DP. Diabetic ketoacidosis: evaluation and treatment. Am Fam Physician. 2013;87(5):337–346.

III. .Koye DN, Magliano DJ, Nelson RG, Pavkov ME. The Global Epidemiology of Diabetes and Kidney Disease. Adv Chronic Kidney Dis. 2018;25(2):121–132. doi: 10.1053/j.ackd.2017.10.011.

IV. .Forouhi NG, Wareham NJ. Epidemiology of diabetes. Medicine (Abingdon) 2014;42(12):698–702. doi: 10.1016/j.mpmed.2014.09.007.

V. Hussain A, Bhowmik B, do Vale Moreira NC. COVID-19 and diabetes: Knowledge in progress. Diabetes Res Clin Pract. 2020;162:108142. doi: 10.1016/j.diabres.2020.108142.

VI. Rauf A, Abu-Izneid T, Olatunde A. COVID-19 Pandemic: Epidemiology, Etiology, Conventional and Non-Conventional Therapies. Int J Environ Res Public Health. 2020;17(21):E8155. doi: 10.3390/ijerph17218155. et al. Published 2020 Nov 4.

VII. Bouhanick B, Cracowski J-L, Faillie J-L. Diabetes and COVID-19. Therapies. 2020;75(4):327–333. doi: 10.1016/j.therap.2020.05.006.

VIII. Singh AK, Gupta R, Ghosh A, Misra A. Diabetes in COVID-19: Prevalence, pathophysiology, prognosis and practical considerations. Diabetes Metab Syndr. 2020;14(4):303–310. doi: 10.1016/j.dsx.2020.04.004.

IX. Abdi A, Jalilian M, Sarbarzeh PA, Vlaisavljevic Z. Diabetes and COVID-19: A systematic review on the current evidences. Diabetes Res Clin Pract. 2020;166:108347. doi: 10.1016/j.diabres.2020.108347.

X. Varikasuvu SR, Dutt N, Thangappazham B, Varshney S. Diabetes and COVID-19: A pooled analysis related to disease severity and mortality. Prim Care Diabetes. 2020. S1751-9918(20)30251-5.

XI. .Orioli L, Hermans MP, Thissen JP, Maiter D, Vandeleene B, Yombi JC. COVID-19 in diabetic patients: Related risks and specifics of management. Annales d'Endocrinologie. 2020;81(2-3):101109. doi: 10.1016/j.ando.2020.05.001.

XII. Apicella M, Campopiano MC, Mantuano M, Mazoni L, Coppelli A, del Prato S. COVID-19 in people with diabetes: understanding the reasons for worse outcomes. The Lancet Diabetes and Endocrinology. 2020;8(9):782–792. doi: 10.1016/S2213-8587(20)30238-2.

XIII. Zhang JJ, Dong X, Cao YY. Clinical characteristics of 140 patients infected with SARS-CoV-2 in Wuhan, China. Allergy. 2020;75(7):1730–174. doi: 10.1111/all.14238. et al.

XIV. Guo W, Li M, Dong Y. diabetes is a risk factor for the progression and prognosis of COVID-19 [published online ahead of print, 2020 Mar 31] Diabetes Metab Res Rev. 2020. p. e3319. et al.

XV. .Singh AK, Gupta R, Ghosh A, Misra A. Diabetes in COVID-19: Prevalence, pathophysiology, prognosis and practical considerations. Diabetes Metab Syndr. 2020;14(4):303–310. doi: 10.1016/j.dsx.2020.04.004.

XVI. Stentz FB, Umpierrez GE, Cuervo R, Kitabchi AE. Pro-inflammatory cytokines, markers of cardiovascular risks, oxidative stress, and lipid peroxidation in patients with hyperglycemic crises. Diabetes. 2004;53(8):2079–2086. doi: 10.2337/diabetes.53.8.2079.

XVII. Wang ZH, Kihl-Selstam E, Eriksson JW. Ketoacidosis occurs in both Type 1 and Type 2 diabetes--a population-based study from Northern Sweden. Diabet Med. 2008;25(7):867–870. doi: 10.1111/j.1464-5491.2008.02461.

XVIII. Zhou F, Yu T, Du R. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet. 2020;395(10229):10541062. doi: 10.1016/S0140-6736(20)30566-3. et al.

XIX. Croft A, Bucca A, Jansen JH. First-time Diabetic Ketoacidosis in Type 2 Diabetics With Covid-19 Infection: A Novel Case Series. J Emerg Med. 2020. et al. S0736-4679(20)30699-5

XX. Pal R, Banerjee M, Yadav U, Bhattacharjee S. Clinical profile and outcomes in COVID-19 patients with diabetic ketoacidosis: A systematic review of the literature. Diabetes and Metabolic Syndrome: Clinical Research and Reviews. 2020;14(6):15631569. doi: 10.1016/j.dsx.2020.08.015.

XXI. .Umpierrez GE, Kitabchi AE. Diabetic ketoacidosis: risk factors and management strategies. Treat Endocrinol. 2003;2(2):95108. doi: 10.2165/00024677-200302020-00003.