Type 2 Myocardial Infarction — An Evolving Entity —

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Type 2 myocardial infarction (T2MI) refers to myocardial necrosis caused by an imbalance in myocardial oxygen supply and demand and in the absence of acute coronary thrombosis. Despite growing recognition of this entity, there remains little understanding of the pathophysiology and uncertainty over the diagnostic criteria for this subtype of MI. Alarming, recent studies suggest that a diagnosis of T2MI pertains a prognosis similar to, if not worse than, type 1 MI. With increasing clinical use of high-sensitivity cardiac troponin assays, the frequency of recognition of T2MI is expected to increase. Yet, there remains a scarcity of prospective studies examining this cohort of patients, let alone randomized clinical trials identifying optimum treatment strategies. Further evaluation of the prevalence, pathophysiology and management of this patient cohort is warranted by the scientific community.

Key Words: Optimum treatment; Prospective studies; Type 2 myocardial infarction

Myocardial infarction (MI), referring to irreversible necrosis of cardiac myocytes caused by prolonged ischemia, was first recognized as a clinical entity in 1910 by Obratsov and Strazhesko through their observation of 5 patients.¹ Since then, sizeable progress has been made in our understanding of the pathophysiology, diagnosis and management of the clinical condition. Nevertheless, because of the varying presentations of a MI, in 2007, almost a century after the entity was first recognized, 5 subtypes were introduced. The 2nd subtype, type 2 MI (T2MI), was described as a MI occurring in the setting of a myocardial oxygen supply/demand mismatch and in the absence of coronary thrombosis.²

Despite a growing acknowledgment of T2MI, very little is still known about the pathophysiology, prognosis and management of this condition. The term has been subject to much confusion and there has been a reluctance to utilize the term in clinical practice.

In the USA, there are significant coding, billing and policy level implications because there is a lack of clarity regarding how to categorize T2MI in the International Classification of Diseases and in the Hospital Readmission Reduction Program,³ where hospitals are financially penalized if they have higher than anticipated risk-standardized 30-day readmission rates for acute MI (AMI).

Alarming, a diagnosis of T2MI can have significant implications for a patient, with accumulating evidence suggesting a prognosis similar to that of patients with type 1 MI (T1MI).^{4,5} Herein, there is increasing urgency to further characterize this cohort and establish evidence-based management strategies. In this setting, we provide a review of the literature available to date and outline future directions that we believe are warranted.

History of T2MI

The first clinical description of MI originated in 1910 when Obratsov and Strazhesko linked the formation of a coronary thrombus with the associated clinical features.¹ Yet, it was a further 30 years before the concept of MI occurring in the absence of thrombus was accepted. In an autopsy study of deceased MI patients, Friedberg and Horn demonstrated an absence of coronary thrombus in 31% of patients, thus fashioning recognition for this entity.⁶ A unified definition of MI was introduced in 1971, when the World Health Organization established a primarily ECG-based definition. With the introduction of biomarkers into clinical practice, this was followed by a collaborated definition of MI in 2000 from the European Society of Cardiology (ESC) and the American College of Cardiology (ACC), which incorporated cardiac troponin.⁷ More recently, the Joint ESC/ACCF/AHA/WHF (American College of Cardiology Foundation/European Society of Cardiology/American Heart Association/World Heart Federation) Task Force for the Redefinition of MI developed the 2007 Universal Definition of MI consensus document that introduced 5 novel subtypes of MI;² which were then preserved in the 2012 revision.⁸

Definition

There was no standardized definition of T2MI until 2007, when a joint Task Force of the ACC/AHA/ESC and the WHF set forth the seminal Universal Definition of MI and in doing so, defined 5 subtypes of MI, including T2MI.²

The 2nd Universal Definition of MI, published in 2012, further clarified the definition of MI: myocardial necrosis

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Table 1. Types of MI

Type of MI	Characterization
Type 1	Spontaneous plaque rupture, ulceration, fissuring, erosion, or dissection with resultant intraluminal thrombus, cessation of myocardial blood flow, and acute myocyte necrosis
Type 2	Ischemic myocardial necrosis resulting from a marked increase in myocardial oxygen demand or a marked decrease in myocardial blood flow, occurring in the absence of acute plaque rupture or coronary thrombosis
Type 3	Sudden cardiac death related to coronary arterial thrombosis
Type 4	MI secondary to percutaneous coronary intervention
Type 5	MI secondary to coronary artery bypass grafting

MI, myocardial infarction.

in a clinical setting consistent with acute myocardial ischemia, in which there is a rise and/or fall of cardiac troponin with at least one value above the 99th percentile of a normal reference population, and the presence of at least one of the following: (1) symptoms of ischemia, (2) new or presumed new significant ST-segment or T-wave changes or new left bundle-branch block, (3) development of pathological Q waves in the ECG, (4) imaging evidence of new loss of viable myocardium, such as a new regional wall motion abnormality, and (5) identification of an intra-coronary thrombus by means of angiography or autopsy.⁸

The Task force outlined 5 subtypes of MI.⁸ T1MI is characterized by plaque rupture, ulceration, fissuring, erosion, or dissection in the setting of atherosclerotic coronary artery disease (CAD), with resultant intraluminal thrombus, cessation of myocardial blood flow, and acute myocyte necrosis.⁸ T2MI is myocardial necrosis resulting from an increase in myocardial oxygen demand and/or a decrease in myocardial blood flow, occurring in the absence of acute plaque rupture or coronary thrombosis.⁸ Type 3 MI refers to sudden cardiac death related to coronary arterial thrombosis. Types 4 and 5 MI are associated complications of percutaneous coronary intervention (PCI) and coronary bypass surgery, respectively.⁸ However, there are several areas of uncertainty over the diagnostic criteria for T2MI, with no formal direction in the consensus statements and guidelines to date.^{8–10} Under these circumstances, a variety of diagnostic criteria have been proposed by the research community. Saaby et al proposed stringent criteria that required the presence of one of the following clinical features to meet the diagnosis: (1) severe anemia defined as hemoglobin <5.5, (2) shock defined as systolic blood pressure <90 mmHg together with signs of organ dysfunction (i.e., metabolic acidosis, arterial oxygen tension <8 kPa, oliguria [diuresis <30 mL/h for at least 3 h], or encephalopathy), (3) bradyarrhythmias requiring medical treatment or pacing, (4) coronary embolism in the presence of a vegetation or ventricular thrombus, (5) respiratory failure with an arterial oxygen tension <8 kPa and clinical signs of acute respiratory failure lasting ≥20 min, (6) ventricular tachyarrhythmia lasting ≥20 min, (7) supraventricular tachycardia lasting ≥20 min with a ventricular rate >150 beats/min, (8) hypertensive pulmonary edema defined as the presence of a systolic blood pressure >160 mmHg, signs of pulmonary edema, and a need for treatment with nitrates or diuretics, or (9) arterial hypertension with systolic blood pressure >160 mmHg and concomitant left ventricular hypertrophy identified by echocardiography or ECG.^{11,12} In contrast, Sandoval et al¹³ proposed the necessity of acute or sustained supply/demand imbalance in the absence of other underlying conditions that lower the ischemic

threshold, such as flow-limiting CAD. However, those authors recommended a more individualized diagnostic approach in patients with lower ischemic thresholds, such as those with obstructive CAD. Sandoval and colleagues argue that a T2MI is often multifactorial; thus, utilizing strict criteria may be an ineffective diagnostic approach.¹³ Furthermore, the threshold at which a patient may suffer a T2MI may vary, reflecting the inherent heterogeneity of the cohort, especially in the presence or absence of CAD. For example, a patient with significant obstructive CAD at baseline may suffer a T2MI in the setting of anemia and a hemoglobin of 7 while a patient with normal coronary arteries may not develop a T2MI unless their hemoglobin drops much lower to <5.5, as suggested by Saaby et al.^{11,12} In our opinion, more personalized criteria may more accurately describe T2MI, but a clarification in the next version of the Universal Definition of MI would be helpful.

Distinguishing T1MI from T2MI can often be challenging in clinical settings. Patients with T1MI usually present with spontaneous symptoms of ischemia with or without associated ischemic ECG changes and in the absence of a clear precipitating cause for increased myocardial oxygen demand. As patients with T1MI may often develop hemodynamic instability, the temporal sequence of events is often crucial for differentiating the 2 entities. Importantly, physicians should be cautious in labelling an MI as a T2MI if an obvious factor that would alter the patients supply/demand balance cannot be readily detected. To further complicate matters, patients may present with more than 1 type of MI concurrently or sequentially (Table 1).⁸

Another important delineation is differentiating T2MI from non-ischemic myocardial injury, because these 2 entities are often confused in clinical practice. This confusion is compounded by the inclusion of “multifactorial” or “indeterminate myocardial injury” in the Third Universal Definition of MI, as several disease processes can instigate this, examples of which include troponin leakage, apoptosis and exocytosis of cytosolic blebs containing troponin.¹⁴ Crucially, in order to be classified as a T2MI, there must be evidence of myocardial ischemia.⁸ Thus, a patient with T2MI should have symptoms of ischemia such as angina or dyspnea and/or evidence of ischemia on ECG such as a ST-segment depression in 2 contiguous leads or new T-wave inversions. Furthermore, a rising or falling troponin level as opposed to a less dynamic pattern of elevation is needed. Non-ischemic myocardial injury can be seen in a variety of settings such as heart failure, renal failure, myocarditis and sepsis.^{8,15–17} These conditions can also cause a rise and fall in troponin; however, importantly they occur without evidence of ischemia as suggested by characteristic symptoms or ischemic findings on ECG. Elevations of

troponin may be mediated by circulating cytokines (sepsis-induced), vasopressors, and catecholamine toxicity.^{8,18,19}

Heart failure deserves a notable mention, as elevation in cardiac troponin can be seen in both acute and chronic heart failure. Crucially, in patients with acute heart failure and elevated troponin levels, a T1MI should always be considered as a possible instigator of the exacerbation. Furthermore, a concurrent T2MI can also be present in an acute heart failure exacerbation because of hemodynamic changes such as tachycardia, hypotension or hypoxemia. In chronic stable heart failure patients, elevations in troponin may be facilitated by chronic myocardial strain with resultant myocyte death. Troponin elevation in this context should be considered as non-ischemic myocardial injury.

Epidemiology

With an aging population of patients with complex medical comorbidities predisposed to demand ischemia,²⁰ it is anticipated that the prevalence of T2MI will increase. In addition, the introduction of high-sensitivity troponin assays into clinical practice is also expected to contribute to an increased recognition of T2MI, and an improvement in accuracy in the lower concentration range may result in improved diagnostic performance.²¹ Epidemiological data to date on T2MI has reported a significant variation in its prevalence and incidence. This may reflect a lack of prospective studies or varying application of the Universal Definition diagnostic criteria in the setting of uncertainty.

Several retrospective epidemiological studies have examined the burden of T2MI. The majority of these studies utilized cohorts first identified by troponin measurement or elevation then adjudicated the proportion of T2MI in patients with a clinical diagnosis of MI. The frequency varies greatly, largely dependent on the patient cohort included and the exact definition applied to define T2MI. In the aforementioned study of 4,499 consecutive, newly admitted patients with cardiac troponin measured by Saaby et al, 533 patients (8.4%) were adjudicated to have a MI, 144 (26%) of which were deemed to be a T2MI.¹¹ Uniquely, the investigators of that study predefined T2MI with the stringent criteria mentioned previously. Baron et al²² analyzed the proportion of T2MI in 19,763 AMI patients admitted to a cardiac or medical intensive care unit (ICU) in 73 Swedish hospitals. T1MI comprised 88.5% of the cases and only 7.1% were classified as T2MI.²² The low prevalence of T2MI reported in that study likely reflects the location in which this study was undertaken; viz., the cardiac or medical ICU. One would expect a large proportion of T2MI cases would be managed in the general medical wards, occurring with or without requirement of an ICU admission. In contrast, T1MI patients are more likely to be managed in the cardiac care units. Studies evaluating patients with acute ischemic symptoms as their main complaint tend to have a lower frequency of T2MI. In a retrospective study by Stein et al examining 2,818 acute coronary syndrome (ACS) patients admitted to a general medicine or a cardiology ward, the proportion of MI patients with T2MI remained low at 4.5%.²³ However, patients in the medical ICU were not included in their study. Similarly, Szymański et al found the frequency of T2MI to be low (2%) in their retrospective study of 2,882 patients who presented to the emergency department (ED) with an initial diagnosis of ACS.²⁴ Yet, their study is also not without limitations, as the authors diagnosed T2MI as an MI occurring 'when there were no

Table 2. Instigating Factors for Type 2 Myocardial Infarction

Increased myocardial demand	Decreased myocardial supply
Hypotension	Hypotension
Sepsis	Anemia
Tachyarrhythmia	Hypoxia
Hypertension	Coronary vasospasm
Thyrotoxicosis	

signs of haemodynamically significant stenosis of atherosclerotic origin in coronary arteries'. The authors' exclusion of patients with hemodynamically significant stenosis is not consistent with the Universal Definition of T2MI.⁸ Using contrasting methodology, Meigher et al examined the prevalence of T2MI in 1,310 patients presenting to the ED and found to have an elevated troponin. T2MI made up 35.2% of patients with an elevated troponin, outnumbering T1MIs (26.5%).²⁵ However the investigators state that a further 35.7% of patients with elevated troponin were "multifactorial" and 2.5% were due to non-ischemic myocardial injury.²⁵ The large proportion of multifactorial troponin elevations reported by those authors limits our interpretation of their results. Smith et al²⁶ examined the incidence of T2MI in 662 patients presenting to the ED with symptoms of ischemia; 139 patients were adjudicated to have a MI, with T2MI comprising 71% of this cohort. Thus, the prevalence of T2MI in retrospective studies has differed substantially with the contrasting methodologies and diagnostic criteria used in each study.

Few prospective studies have examined the incidence and prevalence of T2MI. In a large prospective study, Javed et al examined the prevalence of T2MI in 701 patients presenting to the ED and found to have an elevated troponin. Of this cohort, 216 met the diagnostic criteria for MI, of which 143 (66.2%) had a T1MI and 64 (29.6%) had T2MI.²⁷ Only 2 studies prospectively followed a cohort of patients in order to establish the incidence of T2MI in post-catheterization follow-up cohorts. Morrow et al surveyed 13,608 patients randomized to prasugrel or clopidogrel after ACS with PCI, who were enrolled in the Trial to Assess Improvement in Therapeutic Outcomes by Optimizing Platelet Inhibition with Prasugrel-Thrombolysis in Myocardial Infarction (TRITON-TIMI) 38.²⁸ During a follow-up of 15 months, 3.5% of the cohort developed T2MI.²⁸ In a more recent study of 1,251 patients undergoing coronary or peripheral angiography enrolled in the catheter-sampled blood archive in cardiovascular diseases (CASABLANCA) study, our group found a similar rate of T2MI (12.2%) over a median follow-up of 3.4 years.⁵

Pathophysiology and Patients' Characteristics

The pathophysiology of T2MI is characterized by myocardial necrosis resulting from ischemia caused by either increased myocardial oxygen demand and/or decreased myocardial oxygen supply. Frequently, both processes are involved to varying degrees. Several clinical pathologies can instigate a T2MI (Table 2). Myocardial supply is determined by both the oxygen-carrying capacity of the blood and coronary blood flow. Causes of reduced myocardial supply include: (1) decreased oxygen content of the blood because of hypoxia or anemia, and (2) decreased coronary artery

Table 3. Prognostic Studies of Type 2 Myocardial Infarction

Authors	Study design	Study population	Findings
Saaby et al ¹²	Retrospective study	3,762 hospitalized patients with an elevated troponin	During a median of 2.1 years follow-up, T2MI mortality rate was 49% compared with 26% in patients hospitalized with a T1MI (P<0.0001)
Baron et al ²²	Retrospective study	20,138 patients hospitalized with AMI of which 7.1% had a T2MI	1-year mortality rates were higher in patients who suffered a T2MI as compared with T1MI patients (24.7% vs. 13.5%, P<0.001)
Stein et al ²³	Retrospective study	2,818 patients with AMI	Mortality rates were substantially higher among patients with T2MI compared with those with a T1MI, at both 30-day (13.6% vs. 4.9%, P<0.0001) and 1-year (23.9% vs. 8.6%, P<0.0001) follow-up
Chapman et al ²⁹	Retrospective study	2,122 patients with elevated troponin	5-year all-cause mortality rates were higher in patients with T2MI compared with T1MI (62.5 vs. 36.7%)
Bonaca et al ⁴	Prospective study	13,608 patients with ACS	Cumulative incidence of cardiovascular death at 180 days was comparable between T1MI and T2MI (8.3% vs. 7.3%). T2MI had higher mortality rates when compared with no MI (7.3% vs. 1.3%, P<0.001)
Gaggin et al ⁵	Prospective study	1,251 patients referred for coronary angiography	T2MI was predictive of subsequent MACE (adjusted HR, 1.90; 95% CI, 1.46–2.48; P<0.001), all-cause death (adjusted HR, 2.96; 95% CI, 2.01–4.36; P<0.001), and cardiovascular death (adjusted HR 2.16; 95% CI, 1.36–3.43; P=0.001)

ACS, acute coronary syndrome; AMI, acute myocardial infarction; CI, confidence interval; HR, hazard ratio; MACE, major adverse cardiovascular event; T1MI, type 1 myocardial infarction; T2MI, type 2 myocardial infarction.

perfusion caused by hypotension, bradycardia or coronary vasospasm.

Myocardial oxygen demand is largely determined by systolic wall tension, contractility, and heart rate. In patients with tachyarrhythmias, an increased heart rate decreases ventricular filling time with resultant reduced coronary artery perfusion during diastole. Patients with hypotension need increased ventricular contractility to maintain mean arterial pressure and resultant cell perfusion. In order to facilitate this contractility requirement, an increase in supply to cardiac myocytes is necessary. In patients with hypertensive urgency, systolic wall tension increases in the ventricles according to law of Laplace, increasing cardiac myocyte demand. When such a mismatch in myocyte supply/demand occurs, ischemia ensues and if severe it leads to myocardial necrosis and subsequent troponin elevation.

In a comparative analysis of 2,818 patients with either T1MI or T2MI, Stein et al found that the main precipitants of T2MIs were anemia (31%), sepsis (24%), and arrhythmia (17%).²³ They found that patients with T2MI tended to be older (75.6±12 vs. 63.8±13, P<0.0001), mainly female (43.3% vs. 22.3%, P<0.0001), more frequently have impaired functional level (45.7% vs. 17%, P<0.0001) and have a higher GRACE risk score (150,632 vs. 110,635, P<0.0001).²³ In the CASABLANCA study, patients with T2MI were older (71.3±11.4 vs. 66.2±11.4, P<0.001), had lower diastolic blood pressure (69.3±10.6 vs. 72.9±11.7, P<0.001), and had a higher prevalence of CAD (71.1 vs. 50.1, P<0.001), prior MI (34.2 vs. 22.0, P<0.001), heart failure (36.8 vs. 18.2, P<0.001), peripheral arterial disease (42.8 vs. 24.0, P<0.001), diabetes (46.7 vs. 25.2, P<0.001) and chronic kidney disease (34.2 vs. 10.5, P<0.001) at baseline.⁵

Interestingly, the documented prevalence of obstructive CAD is quite variable in patients with T2MI, depending on cohort demographics, pool of candidates and method of CAD determination such as coronary angiography and definition vs. medical history. In Saaby et al's study, nearly 50% of the patients with a T2MI had normal coronary angiography.¹² In the CASABLANCA study, patients with incident T2MI were more likely to have more diffuse

CAD; for example, those with incident T2MI were more likely than those without to have ≥30% stenosis in at least 2 major coronary arteries (76.0% vs. 59.2%, P<0.001).⁵ The role of pre-existing CAD continues to be an area of great interest in T2MI.

Prognosis

Accumulating studies have assessed the prognostic implications of a diagnosis of T2MI (Table 3). Those published to date suggest that the prognosis of T2MI is similar to, if not worse than, that of a T1MI.

In a retrospective study by Saaby et al of 3,762 hospitalized patients with an elevated troponin, the group found that 119 patients met a diagnosis of T2MI.¹² During a median of 2.1 years follow-up, the group found that the T2MI mortality rate was 49% compared with 26% in patients hospitalized with a T1MI (P<0.0001).¹² In their multivariable Cox regression analysis, current or prior smoker, high age, prior MI, T2MI, hypercholesterolemia, high p-creatinine, and diabetes mellitus were independently associated with death. The adjusted hazard ratio (HR) for T2MI was 2.0 (95% confidence interval (CI), 1.3–3.0).¹² Similar mortality rates were seen in other retrospective studies. Baron et al examined 20,138 patients hospitalized with AMI of which 7.1% of patients had a T2MI.²² Again, 1-year mortality rates were higher in patients who suffered a T2MI as compared with T1MI patients (24.7% vs. 13.5%, P<0.001).²² In a comparative analysis of patients with T1MI and T2MI who participated in 2 prospective national Acute Coronary Syndrome Israeli Surveys (ACSIS) between 2008 and 2010, Stein et al found that mortality rates were substantially higher among patients with T2MI compared with those with a T1MI both at 30-day (13.6% vs. 4.9%, P<0.0001) and 1-year (23.9% vs. 8.6%, P<0.0001) follow-up.²³ The longest follow-up was documented by Chapman and colleagues, where the 5-year all-cause death rates were higher in patients with T2MI compared with T1MI (62.5 vs. 36.7%).²⁹ The increased all-cause death rates were mainly because of a more than double increase in the risk of

Figure. Cumulative hazard curves for major adverse cardiovascular event (A), all-cause death (B), and cardiovascular death in patients after incident type 2 myocardial infarction (C). MACE, major adverse cardiovascular event; MI, myocardial infarction. (Reproduced with permission from Gaggin HK, et al.⁵)

non-cardiovascular death rather than cardiovascular death.

Prospective studies of relatively unselected patients have reported comparable outcomes. In an analysis of the TRITON-TIMI 38 trial, T2MI had a 3-fold increased risk compared with those without MI (adjusted HR: 2.8; 95% CI: 0.9–8.8; $P=0.085$).⁴ The cumulative incidence of cardiovascular death at 180 days was comparable between T1MI and T2MI (8.3% vs. 7.3%).⁴ T2MI had significantly worse

mortality rates when compared with no MI (7.3% vs. 1.3%, $P<0.001$).⁴

In the CASABLANCA study, patients who developed T2MI during follow-up had a significantly poor prognosis (Figure).⁵ Patients with T2MI had higher rates of subsequent adverse events than those without T2MI [per 100 person-years: major adverse cardiovascular event (MACE) 53.7 vs. 21.1, $P<0.001$; all-cause death, 23.3 vs. 3.3, $P<0.001$;

cardiovascular death, 17.5 vs. 2.6, $P<0.001$; heart failure events, 22.4 vs. 7.4, $P<0.001$].⁵ These rates were similar to those seen in patients with T1MI. An incident diagnosis of T2MI was robustly predictive of subsequent MACE (adjusted HR, 1.90; 95% CI, 1.46–2.48; $P<0.001$), all-cause death (adjusted HR, 2.96; 95% CI, 2.01–4.36; $P<0.001$), and cardiovascular death (adjusted HR 2.16; 95% CI, 1.36–3.43; $P=0.001$).⁵

Management Strategies

Unfortunately, the management of T2MI remains uncertain and there are no definitive management strategies available to date.^{8–10} As the reversible factors for T2MI are the precipitating factors, initial management in the acute setting begins with treating the precipitating factor of the supply/demand imbalance. For patients with hypotension and/or sepsis, volume resuscitation and antibiotics may be necessary. Patients with anemia or those with acute gastrointestinal bleeds will require appropriate blood transfusions. Tachyarrhythmias will necessitate rate or rhythm control agents and hypoxemic patients will need respiratory support.

In the absence of evidence, the role of traditional cardiovascular therapies remains unclear. However, observational evidence suggests that medical therapy may actually have limited benefit. For example, results from the CASABLANCA study, demonstrated that, compared with patients who did not suffer a T2MI, patients with T2MI were more likely to be already prescribed conventional cardiovascular therapies, including β -blockers (81.6% vs. 69.1%, $P=0.002$), angiotensin-converting enzyme inhibitors/angiotensin-receptor blockers (64.5% vs. 53.8%, $P=0.01$), aldosterone antagonists (7.2% vs. 4%, $P=0.07$), nitrates (32.3% vs. 17.5%, $P<0.001$), statins (82.9% vs. 72%, $P=0.005$), warfarin (23.3% vs. 14.3%, $P=0.004$) and clopidogrel (30.9% vs. 23.4%, $P=0.04$).⁵ In the TRITON-TIMI 38 trial, prasugrel as compared with clopidogrel did not reduce the incidence of subsequent T2MI in ACS patients undergoing PCI over a 15-month follow-up, albeit rates of T2MI were low among both groups.²⁸ Prasugrel did decrease the incidence of T1MI in this cohort.

In terms of revascularization, Stein et al demonstrated that patients with T2MI were less likely to be referred for coronary interventions (36% vs. 89%, $P<0.0001$).²³ The role of coronary revascularization in this cohort is unclear. Studies to date indicate that obstructive CAD is present in 50–80% of patients following a T2MI.^{12,27,30} Functional evaluation of myocardial perfusion following T2MI is a reasonable option, with the caveat that there is currently no evidence that treating obstructive disease in this cohort is beneficial.

Future Directions

Despite growing concerns over the prognosis of this cohort, there remains a dearth of research regarding their management. Further clarification of the diagnostic criteria for a T2MI is needed. Physicians and researchers need standardized diagnostic criteria to enable consistent analysis of clinical outcomes. Although suggestions have been made on diagnostic criteria to date, these have not been widely accepted. Until a standardized definition is determined the true incidence of the entity cannot be elucidated. The next step would be to further characterize these patients

to facilitate risk stratification and provide clues about underlying pathophysiology, leading to treatment options.

Most importantly, randomized controlled trials are urgently needed to establish evidence-based management strategies. The utility and timing of the administration of traditional cardiovascular therapies such as antiplatelet therapy, statins and β -blockers needs further investigation. Lastly, the value of revascularization in those with obstructive coronary disease will also need exploration.

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