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ST-elevation myocardial infarction late-presenting patients: time for a new paradigm?

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Abstract

Timely performed percutaneous coronary angioplasty (PCI) remains the most critical factor predicting favorable outcomes in patients with ST-elevation myocardial infarction (STEMI). Guidelines have traditionally identified the first 12 hours from symptom onset as the "golden window" for PCI. However, recommendations for patients presenting beyond this timeframe remain inconsistent. Late presenters are associated with worse outcomes and significantly higher rates of in-hospital mortality. Notably, the recent COVID-19 pandemic has further increased the prevalence of late presentations. Emerging imaging techniques now offer new opportunities to better characterize both patients and the pathological consequences of late-presented STEMI. Despite this progress, evidence supporting the adoption of imaging-guided strategies remains mixed. These advancements hold the potential to pave the way for personalized management approaches for this heterogeneous patient population soon. In this review, we explore the current evidence regarding the treatment of late presenters and discuss how emerging imaging techniques may transform clinical strategies in this challenging subset of STEMI patients.

Key words: STEMI, myocardial infarction, late presenters, percutaneous coronary intervention, reperfusion injury.

Introduction

In patients presenting with ST-elevation myocardial infarction (STEMI), the prompt execution of percutaneous coronary intervention (PCI) remains unequivocally one of the most crucial determinants of favorable short- and long-term outcomes [1]. Delays in reperfusion therapy are well-documented to correlate with increased mortality rates [2].

While various biomarkers and diagnostic tools have been proposed to refine the identification of ischemic onset [3], the clinical assessment of typical or atypical ischemic symptoms remains the simplest and most widely adopted approach.

Current guidelines, which predominantly derive their recommendations from data collected during the fibrinolysis era, advocate an early invasive strategy within the first 12 hours of symptom onset [4-7]. This time frame has historically been associated with optimal benefit, while alternative approaches are often suggested for so-called late presenters—commonly defined as patients presenting between 12 hours and 28 days after symptom onset. Advances in PCI techniques and imaging modalities, however, are beginning to challenge these established paradigms. These innovations may soon prompt a reevaluation of our current management strategies, potentially reshaping the way we approach late presenters in the near future.

Epidemiology

International databases highlight diabetes, a history of heart failure (HF), and atypical chest pain as strong predictors of late presentation in STEMI patients. However, the role of female gender as a predictive factor remains inconsistent across studies [8-10]. Additional conditions such as prior stroke and cancer also appear to be more prevalent in late presenters, as evidenced by Bouisset et al. in a comprehensive analysis of a national registry [11].

Female gender also plays a role: multiple studies report longer delays in women, primarily due to lower symptom recognition, older age at onset, and more frequent presentation with atypical symptoms such as dyspnea, nausea, and fatigue rather than classic chest pain [12,13].

Pathophysiological differences, including a lower atherosclerotic burden, increased microvascular resistance, and differing plaque characteristics, may contribute to both delayed recognition and increased mortality in women [13]. In addition, lower educational status and cultural perceptions of myocardial infarction as a “male disease” have been associated with greater pre-hospital delays among women [14,15].

Late presenters are less likely to undergo coronary angiography and PCI, and even when treated, their post-procedural angiograms more often reveal suboptimal TIMI flow grades (2–3), reflecting poorer procedural outcomes [9]. A recent retrospective study involving 13,707

patients demonstrated that late presenters have a persistently worse prognosis compared to early presenters, with higher rates of in-hospital mortality and complications such as HF, myocardial rupture, and complete atrioventricular block. This difference extends to a 3-year follow-up, underscoring the long-term impact of delayed presentation [16].

Among late presenters, specific factors have been associated with a particularly poor prognosis, including advanced age, history of stroke, prolonged delays from symptom onset to intervention, anterior STEMI, a high heart rate/systolic blood pressure ratio, and being comatose following resuscitation [17].

Late presentation is not an uncommon phenomenon; up to 20% of STEMI patients fall into this category [8]. Encouragingly, the prevalence of late presentation had been declining steadily until 2019 [16]. However, this trend reversed during the COVID-19 pandemic [18-20]. Many patients avoided hospitals for fear of infection, leading to substantial delays in seeking care—even in low-incidence areas such as Ticino, Switzerland, where symptom-to-call times nearly tripled [21]. Rare complications such as hemorrhagic pericarditis re-emerged due to extreme delays in treatment [22].

The impact of the pandemic on STEMI-related mortality remains controversial [23,24]. While some studies report increased mortality rates, others, including a recent meta-analysis by Kamarullah et al. involving 10,263 STEMI patients across five registries, found no significant difference in in-hospital mortality between late and early presenters during the pandemic [25].

Geographic and socioeconomic disparities critically shape the epidemiology of late presentation. In low- and middle-income countries (LMICs), STEMI patients are often younger and face structural barriers such as limited PCI access, underdeveloped EMS systems, and treatment delays, all contributing to worse outcomes [26]. In high-income countries, access is more uniform, yet income-based disparities persist. A large international study of over 289,000 STEMI patients across six nations showed significantly higher mortality among low-income individuals, with Israel reporting a one-year mortality of 25.3% vs. 16.2% in high-income counterparts [27]. Nonetheless, targeted care models can bridge these gaps. The TN-STEMI Program in India, utilizing a pharmaco-invasive, hub-and-spoke strategy, significantly reduced one-year mortality despite unchanged ischemia times, underscoring the value of system-level solutions in resource-limited settings [28].

Another relevant contributor to late presentation is distance from a PCI-capable center. In an Italian regional cohort, patients with above-median travel times exhibited a 2.5-fold increase in 30-day mortality, despite door-to-balloon times 120 minutes [29]. A U.S. STEMI network reported similar in-hospital mortality (7–8%) for patients transferred from >25 vs. 25 miles, underscoring the mitigating role of coordinated systems [30]. Nonetheless, pre-PCI delays

remain nontrivial: <15% of transferred patients meet the <30-minute door-in–door-out (DIDO) benchmark. To address persistent system delays, the American Heart Association has proposed the "STAT TRANSFER" protocol—a structured, EMS-style activation designed to streamline interhospital handoffs [31].

Physiopathology

The well-established relationship between the timing of coronary blood flow restoration and myocardial tissue salvage stems from pioneering studies conducted on animal models several decades ago [32-34]. These findings laid the groundwork for fibrinolysis to emerge as the cornerstone therapy for STEMI patients [35]. It is now evident that the longer the interruption of coronary blood flow persists, the greater the damage to cardiomyocytes, even when reperfusion is eventually achieved. This is largely attributable to the phenomenon of "reperfusion-associated pathology." During ischemia, the shift to anaerobic metabolism depletes ATP and lowers intracellular pH. Revascularization reintroduces oxygen, triggering reactive oxygen species (ROS) production and rapid pH normalization, which, in turn, opens mitochondrial permeability transition pores. This cascade leads to calcium overload, mitochondrial swelling, cell membrane rupture, and ultimately irreversible cellular damage [36,37].

In murine models of myocardial infarction (MI) using temporary coronary ligation (ischemia-reperfusion models), an ischemic period exceeding two hours results in an infarct size of approximately 30%, a critical threshold beyond which cardiac function is significantly impaired—comparable to permanent coronary occlusion [38]. However, caution is warranted when extrapolating results from such models to humans. For instance, in clinical settings, up to one-third of MI patients experience spontaneous resolution or recanalization of the occluded coronary artery before medical intervention [39,40]. This phenomenon, possibly driven by mechanisms like preconditioning and post-conditioning, may offer myocardial protection and limit necrosis [41]. Moreover, unlike in rats or pigs, collateral circulation in humans can preserve sufficient myocardial perfusion, mitigating damage even during prolonged coronary occlusion. Patients with chronic coronary syndrome often develop robust collateral vessels, which are associated with better outcomes, such as a reduced risk of cardiogenic shock during acute occlusion [42,43].

For late presenters, additional complications, such as microvascular obstruction (MVO) and intramyocardial hemorrhage (IMH), are critical to consider. These phenomena represent the leading causes of angiographic "no-reflow," wherein myocardial tissue remains hypoperfused

despite successful removal of the coronary occlusion. Animal studies have demonstrated a strong association between prolonged ischemia and post-reperfusion IMH [44,45].

With the advent of advanced cardiac magnetic resonance (CMR) imaging, these ischemic complications can now be detected non-invasively in human patients. CMR studies have shown that MVO and IMH frequently coexist in STEMI settings [32,46], with ischemic time being a significant contributor to their development, as observed in both animal and human studies [47,48]. Additionally, the routine use of potent antiplatelet agents post-PCI may exacerbate the extent of IMH [47].

Importantly, MVO is not simply a marker of reperfusion failure but a direct consequence of multifactorial microvascular injury involving endothelial swelling, neutrophil plugging, microembolization, vasoconstriction, and external compression due to edema and hemorrhage [48]. Histopathological and imaging studies have demonstrated that MVO follows a dynamic course, with a peak in extent within the first 48 hours and potential spontaneous resolution over weeks [48,49]. CMR-LGE provides a reproducible method to quantify MVO, which correlates with increased LV volumes and reduced LVEF over time. Segmental strain analysis also shows good diagnostic accuracy for both MVO and LGE [50]. Furthermore, the prevalence of MVO is influenced by both ischemia duration and the timing/mode of reperfusion, with studies showing comparable rates even among patients treated with thrombolysis, rescue PCI, or presenting beyond 12 hours [45].

Quantifying MVO is increasingly recognized as crucial, given its strong association with adverse outcomes such as mortality and HF-related hospitalizations within one year [51].

In summary, delayed reperfusion exacerbates myocardial damage by inducing ischemia-reperfusion injury—a paradoxical process characterized by ROS production, calcium overload, and inflammatory responses triggered by reperfusion itself. The ultimate extent of myocardial salvage and damage results from a delicate interplay of mechanisms, including apoptosis, autophagy, inflammation, and fibrosis, which have been extensively studied in both humans and animal models. Recent research has identified circular RNAs (circRNAs) as important regulatory elements in these processes. These non-coding RNAs, which act as microRNA sponges or bind to RNA-binding proteins, are tissue- and time-specific and have been shown to influence gene expression during different phases of ischemic injury, cardiac healing, and remodeling [52].

Comorbidity and complications

Patients presenting beyond the conventional reperfusion window frequently exhibit a complex profile of comorbid conditions that not only contribute to diagnostic uncertainty but may also

influence pre-hospital delays and clinical outcomes. Among these, diabetes mellitus is one of the most consistently reported independent predictors of late presentation. The pathophysiological rationale includes diabetic autonomic neuropathy and a higher prevalence of atypical or silent ischemia, both of which may impair symptom recognition and delay care-seeking behavior [53-55].

Chronic kidney disease has similarly been implicated in delayed access to care. Although its direct association with late presentation remains less robust, patients with renal dysfunction often carry multiple comorbidities and higher frailty indices, which may render their clinical presentation more insidious and contribute to diagnostic delay. In a cohort of U.S. veterans, those with significant non-cardiac comorbidities—including renal failure—were disproportionately represented among those excluded from early reperfusion pathways [56]. Real-world data from large cohorts suggest that late presenters often exhibit distinct profiles—older age, female sex, diabetes, and no prior revascularization—yet delayed presentation per se may not independently predict worse prognosis, underscoring the heterogeneity of this population and the need for tailored strategies [54,56].

Beyond comorbidities, late presentation in ST-elevation myocardial infarction (STEMI) is closely linked to increased cardiovascular complications and worse in-hospital outcomes, particularly in the presence of cardiogenic shock. In a prospective study, patients presenting 24 hours after symptom onset had significantly higher rates of acute kidney injury (72.7% vs. 41.7%) and major adverse cardiovascular events at discharge (81.8% vs. 45.8%), primarily driven by excess mortality (77.3% vs. 16.7%). Late presenters were more frequently classified as advanced stages of shock (SCAI stage D or E), reflecting greater clinical instability at admission [57,58].

The temporal trajectory of in-hospital death has also been elucidated in the OBTAIN registry. While early deaths (7 days) were associated with ST-elevation, low systolic blood pressure, and cardiac arrest, later deaths (8 days) were more commonly linked to complications such as atrial fibrillation, pulmonary edema, major bleeding, lung disease, and surgical revascularization [58].

Mechanical complications represent a key determinant of late morbidity. Despite advances in reperfusion, patients with large infarcts or delayed care remain at risk of structural sequelae including papillary muscle rupture with acute mitral regurgitation, ventricular septal defect (VSD), free wall rupture, and pseudoaneurysms. These events, though infrequent, are associated with high mortality and resource utilization [59]. Surgical repair remains the gold standard for mechanical complications. Even beyond the optimal window, late revascularization may limit infarct size and remodeling in symptomatic or unstable patients,

while stress imaging can guide management in asymptomatic case [60]. Even beyond the optimal window, late presenters remain vulnerable to rare but life-threatening sequelae such as conduction disturbances. In particular, high-grade atrioventricular block may complicate inferior STEMI with delayed presentation, reflecting ischemia of the conduction system and requiring prompt recognition and supportive pacing to prevent hemodynamic collapse [61].

Does angina matter?

The relationship between the onset of symptoms and the formation of a thrombus in the infarct-related artery is less straightforward than often assumed. Rittersma et al. found evidence of organized, lytic thrombi in nearly half of 211 STEMI patients presenting within six hours of symptom onset, suggesting that the thrombus may have developed days or even weeks earlier [62]. Similarly, a recent study of 97 STEMI patients identified red thrombi in nearly two-thirds of cases and white thrombi—associated with a higher incidence of in-hospital major adverse cardiovascular events (MACE)—in over one-third of cases [63].

In late presenters, the correlation between ischemic time and myocardial salvage appears to weaken. Imaging studies using CMR in high-risk late presenters have demonstrated variability in myocardial salvage despite prolonged ischemic times [64,65]. For example, a previous study of PCI-treated late presenters found only a weak correlation between salvage index, left ventricular ejection fraction, and symptom duration [66].

In this context, CMR emerges as a pivotal tool to characterize myocardial tissue status beyond ischemic time. By assessing edema, necrosis, MVO intramyocardial hemorrhage (IMH), and fibrosis, CMR enables identification of patients with substantial salvageable myocardium even in the late window. A significant proportion of patients presenting 12–48 hours after symptom onset still demonstrate a myocardial salvage index 0.5, suggesting potential benefit from revascularization regardless of delay [64,67]. Longitudinal CMR studies have shown that infarct size may decrease significantly over time, but persistent tissue abnormalities such as iron deposition and edema within the infarct core—present in nearly 30% and 24% of patients respectively—are associated with impaired infarct healing and worse remodeling outcomes [68]. Furthermore, early detection of MVO on CMR has been independently associated with impaired myocardial salvage, even after adjusting for ischemic burden and infarct location, reinforcing its role as a prognostic marker and a potential modifier of post-infarction therapeutic strategies [69].

Innovative tools, such as intracoronary ECG for measuring Q-wave evolution, initially used in early STEMI presenters, could be extended to late presenters to assess myocardial viability and identify patients with salvageable tissue [3,70]. In particular, ST-segment resolution recorded

via intracoronary ECG has been independently associated with microvascular obstruction, infarct size, and adverse left ventricular remodeling as assessed by CMR at 4 and 90 days post-infarction [71]. A recent meta-analysis has also shown that IC-ECG has promising diagnostic accuracy for local myocardial injury, with a pooled sensitivity and specificity of 78% and 87%, respectively [72]. However, a small study involving 66 very late presenters using ECG-based scoring methods revealed only modest correlations with myocardial salvage [73].

Advanced echocardiographic modalities have been explored as potential tools to assess myocardial viability in late presenters. Non-invasive myocardial work indices, derived from speckle-tracking and blood pressure measurements, have shown an inverse relationship with infarct transmurality on CMR, suggesting a possible role in identifying viable myocardial segments [74]. Similarly**,** myocardial contrast echocardiography (MCE**)** allows real-time evaluation of perfusion and has been associated with prediction of functional recovery, although its routine use remains limited. Emerging techniques such as high-frame-rate MCE and echocardiographic ultrasomics have shown promise in detecting subtle perfusion abnormalities and stratifying risk post-infarction [75,76], but their clinical application in this setting remains investigational. In this context, global longitudinal strain (GLS) has shown prognostic value in predicting adverse remodeling after late PCI [77], and techniques such as pulse-cancellation echocardiography have demonstrated concordance with CMR in the identification of myocardial scar [78].

Reperfusion strategy and guidelines

The role of routine primary PCI (pPCI) in late-presenting STEMI patients has been the subject of extensive investigation. Schömig et al. [79], in a trial involving 365 STEMI patients presenting 12–48 hours after symptom onset, demonstrated that an invasive strategy combining PCI and abciximab significantly reduced infarct size as assessed by SPECT. However, no differences were observed in the composite endpoint of death, MI, or stroke at 30 days. The four-year follow-up hinted at a barely significant reduction in mortality in the PCI group [80].

Similarly, Gierlotka et al. [81], in a registry analysis of 2,036 late-presenting patients (12–24 hours), found significantly lower mortality rates in PCI-treated individuals at 12 months. This survival advantage persisted even after multivariable adjustment and propensity score matching.

More recently, Bouisset et al. analyzed data from three nationwide observational registries as part of the FAST-MI program [11]. Among 1,169 late-presenting STEMI patients (12–48 hours after symptom onset), those who underwent PCI had significantly lower all-cause mortality

after a median follow-up of 58 months, even after adjusting for potential confounders. Revascularization was associated with a 35% reduction in adjusted mortality risk; the study's limitations include the lack of data on whether patients were symptomatic at the time of PCI.

Consistent with these findings, the AMIS Plus registry [18], which included 27,231 late-presenting STEMI patients (>12 hours) over two decades, documented a progressive increase in PCI use, particularly in patients presenting within 12–48 hours. This trend was associated with a reduction in in-hospital mortality, with the benefit of PCI persisting even after multivariate analysis.

In contrast, for very late presenters (3–28 days after symptom onset), the Occluded Artery Trial (OAT) and the TOSCA-2 trial demonstrated no benefit of routine PCI in terms of mortality or left ventricular ejection fraction compared to medical therapy alone [82,83]. It is worth noting that these studies were conducted in an era when bare-metal stents were the only option, potentially limiting their applicability to contemporary practice.

More recent real-world data from a Chinese study involving 1,072 STEMI patients with symptom onset between 12 hours and 28 days showed that PCI was associated with lower rates of all-cause and cardiac mortality, even after propensity score matching analyses [84,85]. Table 1 summarizes the key findings from these pivotal trials, highlighting differences in population, intervention, and outcomes.

Current guidelines provide nuanced recommendations for late presenters. The 2023 ESC guidelines endorse pPCI in patients presenting more than 12 hours after symptom onset if unstable (Class I, Level C), and suggest routine PCI for stable patients presenting within 12–48 hours (Class IIa, Level B) [6]. Beyond 48 hours, routine PCI is formally discouraged (Class III, Level A), unless there is evidence of viability or inducible ischemia. Similarly, the 2025 AHA/ACC guidelines limit pPCI beyond 12 hours to patients with ongoing ischemia or hemodynamic instability (Class IIa), while explicitly advising against routine PCI after 48 hours in the absence of symptoms (Class III, Level B) [7]. Key guideline recommendations are summarized in Table 2.

Despite the detailed stratification, several areas of uncertainty remain, particularly regarding the definition of “stable” patients. The term frequently includes those who are asymptomatic at presentation; however, symptom resolution does not necessarily equate to myocardial recovery or absence of risk. In this light, the clinical profile of late presenters—often older, diabetic, or presenting with atypical symptoms—raises questions on whether current definitions adequately capture the heterogeneity of this group. Moreover, existing recommendations are predominantly based on legacy data from the thrombolytic era or from early PCI trials with limited inclusion of patients beyond 48 hours. As noted by recent literature

[85-87], these studies often lacked contemporary stent technologies, optimized pharmacotherapy, and advanced imaging guidance. This restricts their external validity in modern clinical settings. The apparent divergence between ESC (Class III-A) and AHA/ACC (Class III-B) recommendations beyond 48 hours reflects not merely a difference in interpretation, but a deeper knowledge gap. The available evidence, though aligned in discouraging routine PCI in asymptomatic patients beyond this threshold, remains modest in scope and does not fully address imaging-guided or viability-directed strategies. Emerging data suggest that a subset of late presenters—despite being clinically stable—may retain substantial viable myocardium and derive meaningful benefit from revascularization. This is supported by pathophysiological mechanisms such as preserved collateral flow, delayed necrosis, and ischemic preconditioning, and corroborated by CMR and outcome data from trials like BRAVE-2 and FAST-MI [1,81]. Further prospective, imaging-guided investigations are warranted to refine therapeutic algorithms for this complex and underrepresented population. A visual summary of the decision-making process is presented in Figure 1.

Medical therapy

Guideline-directed medical therapy (GDMT) remains fundamental in the management of patients presenting beyond the acute phase. Both the ESC (2023) and ACC/AHA (2025) emphasize the early initiation of dual antiplatelet therapy (DAPT), high-intensity statins, beta-blockers, and renin–angiotensin–aldosterone system (RAAS) inhibitors, irrespective of the timing of presentation [6,7,88]. DAPT with aspirin and a $P2Y_{12}$ inhibitor continues to be a central pillar. Despite the preference for potent agents such as ticagrelor or prasugrel in contemporary guidelines, clopidogrel remains the most commonly employed agent among late presenters. This likely reflects clinical caution in the setting of delayed ischemia, increased bleeding risk, and the absence of direct evidence supporting intensified platelet inhibition in this subset. In FAST-MI, clopidogrel was prescribed in 67.1% of late presenters versus 56.5% of early presenters ($P < 0.001$) [1]. The AMIS Plus registry documented a progressive increase in $P2Y_{12}$ inhibitor use over two decades, surpassing 90% in the most recent cohorts [13]. Similar findings from the French registry further support the prevalent use of clopidogrel in conservatively managed or hemodynamically stable patients [11].

Intravenous antiplatelet agents, including glycoprotein IIb/IIIa inhibitors and cangrelor, may be selectively used in late presenters undergoing PCI, particularly in the presence of high thrombus burden or suboptimal flow. While their routine use has declined, isolated data suggest procedural advantages in anatomically complex cases, though robust evidence in this specific population remains lacking [89]. Anticoagulation follows standard protocols.

Unfractionated heparin and low-molecular-weight heparin (LMWH) remain the preferred options, with bivalirudin reserved for high-bleeding-risk scenarios. In FAST-MI, LMWH was used in over half of late presenters, while bivalirudin was employed in fewer than 3% of cases [1]. Neurohormonal modulation, particularly through RAAS inhibition, plays a pivotal role in secondary prevention. In the Korean Acute Myocardial Infarction Registry, the use of RAAS inhibitors at discharge was associated with a 66% relative reduction in cardiac death or recurrent myocardial infarction at one year, even among patients with preserved left ventricular ejection fraction. Serial echocardiography demonstrated significant improvements in LVEF and reductions in LV end-systolic volume, consistent with attenuation of post-infarct remodeling [90]. Beta-blockers and statins are widely prescribed at discharge. Diuretics, particularly loop agents, are more frequently required in this population, reflecting a higher burden of congestion and left ventricular dysfunction at presentation [1,18].

Conclusions

The management of late-presenting STEMI patients poses a nuanced clinical challenge. While the benefit of early revascularization is well established, this population is far from uniform. Late presenters vary widely in terms of hemodynamic status, infarct characteristics, and comorbidities—calling for a more individualized approach. Emerging imaging tools such as cardiac magnetic resonance, intracoronary ECG, and advanced echocardiography offer an unprecedented opportunity to characterize tissue damage, identify viable myocardium, and guide revascularization decisions. Integrating these modalities into routine care may shift the focus from timing alone to a pathophysiological assessment of salvageability. Medical therapy remains the cornerstone of treatment, but real-world data reflect variations in practice that highlight the need for tailored antithrombotic strategies. Future guidelines should embrace the complexity of this group and support decision-making beyond binary time windows. Time remains muscle — but imaging and clinical stratification can guide us beyond the clock.

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Table 1. Key studies on invasive strategy in late STEMI presenters.

Study	Population	Time window	Intervention	Main findings
Schömig et al. [79]	365 STEMI patients	12–48 hours	PCI + abciximab	Reduction in infarct size (SPECT); no significant difference in mortality, MI, or stroke at 30 days.
Gierlotka et al. [81]	2,036 late presenters	12–24 hours	PCI	Significant reduction in 12-month mortality, persisting after multivariable adjustment and propensity matching.
Bouisset et al. [11]	1,169 late presenters	12–48 hours	PCI	35% lower adjusted all-cause mortality compared to non-revascularized patients; benefit observed at 58-month follow-up.
OAT Trial [83]	Very late presenters (3–28 days)	3–28 days	Routine PCI	No improvement in mortality or LVEF compared to medical therapy alone at 4 years.
TOSCA-2 [84]	381 patients	3–28 days	IRA revascularization	No effect on LVEF at 1 year compared to medical therapy.
AMIS Plus Registry [18]	27,231 late presenters	>12 hours	PCI	Increased PCI use (12–48 hours) over two decades associated with lower in-hospital mortality.

Summary of pivotal studies evaluating the role of PCI in patients presenting beyond 12 hours after STEMI onset. Outcomes vary depending on timing, clinical stability, and imaging guidance. PCI, percutaneous coronary intervention; LVEF, left ventricular ejection fraction; IRA, infarct-related artery; SPECT, single-photon emission computed tomography; MI, myocardial infarction.

Table 2. Key recommendations for late STEMI presenters in ESC and AHA/ACC guidelines.

Guideline	Time window	Recommendation	Class/level of evidence
ESC 2023 Guidelines [6]	>12 hours	PCI for unstable patients with signs of ongoing ischemia.	I/C
	12–48 hours	Routine PCI for stable patients.	IIa/B
	>48 hours	Routine PCI not recommended unless viability or ischemia is demonstrated.	III/A
AHA/ACC 2025 Guidelines [7]	12–24 hours	PCI is reasonable to improve clinical outcomes	IIa/B-NR
	>24 h (with ischemia/arrhythmia/HF)	PCI is reasonable in selected patients	IIa/C-LD
	>24 h (asymptomatic, totally occluded IRA)	Routine PCI not recommended (no proven benefit)	III/B-R

Summary of ESC 2023 and AHA/ACC 2025 guideline recommendations for PCI in late STEMI presenters. Guidance varies based on timing, symptoms, and stability. PCI, percutaneous coronary intervention; HF, heart failure.

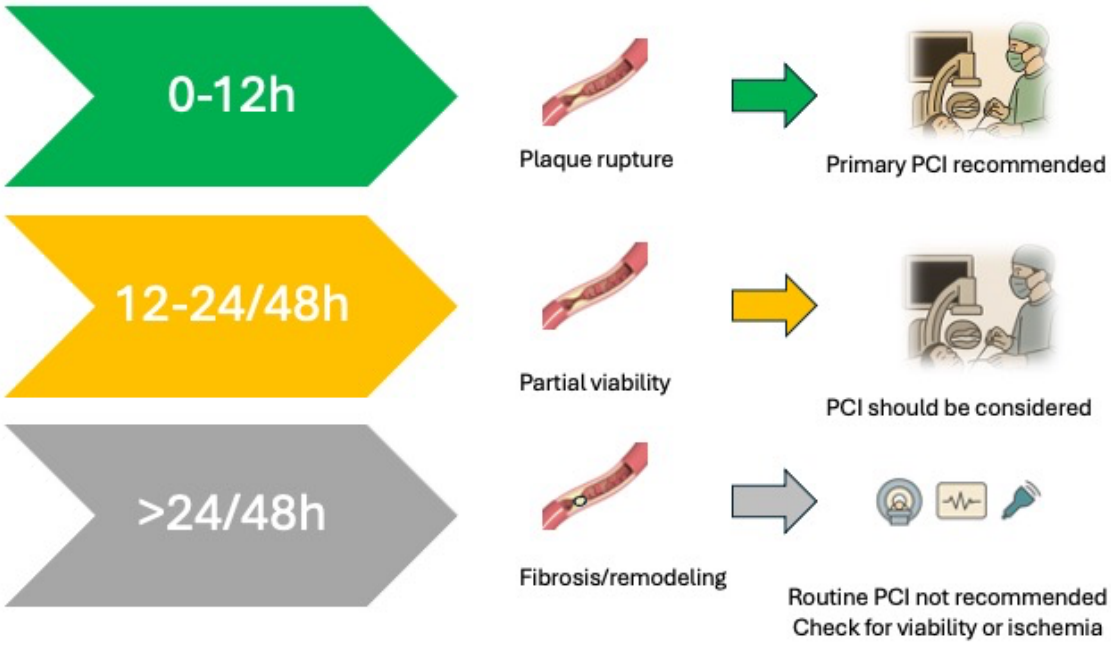

Figure 1. Visual summary of decision-making in late STEMI presentation. Timing since symptom onset (0–12 h, 12–24/48 h, >24/48 h) guides PCI strategy based on underlying pathophysiology—ranging from plaque rupture to fibrosis—and highlights the role of advanced imaging in selected cases. PCI = percutaneous coronary intervention.