EDITORIAL

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Turning evidence into action: the real challenge of guideline-directed medical therapy in acute myocardial infarction

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Acute myocardial infarction (AMI) remains the leading cause of cardiovascular morbidity and mortality worldwide, necessitating comprehensive therapeutic approaches that extend beyond primary percutaneous coronary interventions (PCI). Guideline-directed medical therapy (GDMT) has become the cornerstone of contemporary cardiovascular care, significantly improving outcomes in this patient population. The concept of GDMT originated from the evidence-based clinical practice framework systematized by Eddy in the 1980s [1]. GDMT has since been refined through numerous landmark trials and is now a core therapeutic strategy, particularly for heart failure with reduced ejection fraction (HFrEF), where the modality has demonstrated significant benefits in reducing mortality and hospitalizations [2]. Although originally developed in the context of HFrEF, the GDMT principles have been extended to the management of AMI with endorsement from leading cardiovascular societies. Importantly, the GDMT is not merely a collection of recommended agents; the modality represents a structured, evidence-based treatment paradigm aimed at improving survival, preventing complications, and promoting long-term cardiovascular health.

In the AMI setting, the GDMT includes a broad spectrum of interventions beyond heart failure management. These include potent antiplatelet and anticoagulant therapies to mitigate the acute thrombotic risk, intensive lipid-lowering strategies, and targeted protocols for complications, including cardiogenic shock. Given that AMI is a major precursor to heart failure, GDMT in AMI often overlaps with HFrEF management, particularly through foundational therapies such as beta-blockers and renin–angiotensin–aldosterone system (RAAS) inhibitors. Thus, GDMT for AMI should be implemented from a longitudinal treatment perspective, encompassing both acute-phase interventions and comprehensive secondary prevention strategies to reduce recurrence, delay the progression of heart failure, and improve overall cardiovascular outcomes.

Consistent evidence has demonstrated that GDMT adherence at discharge and during follow-up was strongly associated with a reduced risk of major adverse cardiovascular events, including mortality and coronary revascularization [3-6]. A notable finding from the Korean multicenter KAMIR-NIH registry revealed that GDMT significantly reduced 3-year cardiac mortality from 8.6% to 5.0% (sub-distribution hazard ratio [HR], 0.53), and non-cardiac mortality from 4.5% to 3.2% (HR, 0.69). Using the restricted mean time lost methodology, GDMT was associated with a gain of 28.5 days of cardiac life and 8.9 days of non-cardiac life over 3 years [6]. These findings suggest that the benefits of GDMT extend beyond direct cardiac protection, potentially through mechanisms such as reduced thromboembolism, kidney protection, or the pleiotropic effects of medications commonly administered following AMI, including statins or RAAS inhibitors, which exert anti-inflammatory, endothelial-stabilizing, and anti-atherosclerotic properties. This broad systemic effect underscores the comprehensive health benefits of GDMT.

Despite these benefits, the real-world adherence to GDMT remains suboptimal. In Korea, the utilization of GDMT declined from 70.2% at the time of hospital discharge to

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54.6% at the 3-year follow-up [6]. The barriers to sustained implementation of GDMT are multifactorial, encompassing patient-related factors (e.g., high cost of agents such as proprotein convertase subtilisin/kexin type 9 inhibitors, comorbidities, and limited health literacy), provider-related factors (e.g., clinical inertia, knowledge gaps, and time constraints), and system-level factors (e.g., fragmented care models, inadequate reimbursement, and limited access to cardiology specialists) [7]. To improve the real-world implementation of GDMT, clinicians and healthcare systems must adopt a structured multilevel strategy [8,9]. For cardiologists, comprehensive discharge planning is essential—prescribing foundational GDMT components unless contraindicated, as omission of a single agent may result in a loss of approximately 37.8 days of survival over 3 years [6]. For general physicians, long-term surveillance is crucial as GDMT adherence commonly declines after the first year post-AMI [4]. Comorbidity management, including renal function, cancer screening, and infection prevention, is integral given GDMT's potential multi-system benefits. In frail older patients, careful risk-benefit assessment is needed to minimize adverse effects such as orthostatic hypotension, bradyarrhythmia, or bleeding [8,9]. Embedding GDMT dashboards into electronic medical records may improve consistency, while incentive-based payment models, such as those rewarding ≥ 90% GDMT prescription at discharge—which have already proven effective in heart failure care—could be adapted to improve adherence in the management of AMI [2]. Central to all these efforts is the early inpatient initiation of GDMT with dose titration every 1–2 weeks as tolerated. Patient education remains critical for addressing common side effects (e.g., transient fatigue or dizziness) and preventing premature discontinuation. Multidisciplinary care teams, including cardiologists, nurses, and pharmacists, are critical for optimizing therapy, especially in complex cases such as those of cardiogenic shock. In addition, participation in cardiac rehabilitation has been demonstrated to support improved long-term compliance. Finally, digital health tools can aid medication monitoring and reinforce adherence, making GDMT delivery significantly effective and patient-centered [10].

Future research on GDMT should focus on improving how treatments are adjusted and personalized for each patient. First, more studies are needed to better understand the application of GDMT in patient populations underrepresented in previous randomized trials, such as those with preserved cardiac function after PCI. These studies can help reduce unnecessary medication use while maintaining clinical benefits. Second, new biological studies utilizing tools such as gene expression profiling and proteomic analysis may help elucidate the mechanisms through which GDMT confers mortality benefits beyond cardiac protection, including renal preservation and anti-inflammatory effects. Finally, since non-cardiovascular deaths become increasingly prevalent after 6–7 years, future registries should include long-term follow-up using competing-risk models. These extended analyses will help clarify the long-term impact of GDMT on patient outcomes.

In summary, GDMT is not merely a protocol but also a transformative tool for improving outcomes in AMI. GDMT reduces mortality and mitigates the burden of recurrent events by targeting diverse pathophysiological pathways with a comprehensive array of pharmacological agents. Ensuring the broader adoption of GDMT requires collaborative, patient-centered care and a system-wide commitment to its implementation. Moving forward, bridging the gap between evidence and practice remains a critical challenge and valuable opportunity in contemporary cardiovascular care.

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