



Sharing the Care: Managing the Myocardial Infarction Patient Postdischarge

Learning Objectives

After completing this activity, participants should be better able to:

- Apply evidence-based treatment guidelines to the long-term management of patients discharged from the hospital after experiencing myocardial infarction (MI)
- Identify common barriers to treatment adherence in patients with MI
- Formulate strategies for educating patients with MI on the need for long-term therapy to prevent recurrent events

Introduction

Patients who survive their first myocardial infarction (MI) are at high risk (up to 15 times higher than the general population) of having another cardiovascular (CV) event and dying from it.¹ Evidence-based treatment guidelines for the postdischarge care of patients with MI stress the importance of platelet inhibition, β -blockade, angiotensin-converting enzyme (ACE) inhibition, and statin therapy for long-term management.²⁻⁴ Adherence to treatment guidelines has been shown to reduce short- and long-term mortality.⁵

However, only 74% of patients fill all their discharge prescriptions after hospitalization for acute MI,⁶ and an even smaller proportion use these medications consistently over the long term.⁷ Thus, appropriate transition from the inpatient hospital setting to outpatient care is a critical factor in improving patient outcomes after MI. Primary care clinicians need to ensure appropriate medication use, provide any needed treatment adjustments, and counsel patients on the importance of secondary prevention measures as part of their ongoing care.

This learning module will focus on the immediate and long-term management of patients with MI after hospital discharge, including adhering to guideline recommendations for secondary prevention of recurrent ischemic events, optimizing therapy, overcoming barriers to treatment adherence, and providing ongoing patient education. Strategies for effectively managing patients after MI also are illustrated in a case study of a patient hospitalized for acute MI (see page 10).

Only 74% of patients fill all their discharge prescriptions after hospitalization for acute MI, and an even smaller proportion consistently use these medications.

Evidence-Based Treatment Guidelines

Adherence Improves Survival

According to practice guidelines from the American Heart Association (AHA) and the American College of Cardiology (ACC), all patients who have experienced an MI—regardless of the intervention used to manage the acute event (eg, stenting, coronary artery bypass grafting [CABG], or medical therapy alone)—require long-term dual antiplatelet therapy, β -blockade, ACE inhibition, and statin therapy for secondary prevention (Figure 1).^{2,4} Increased adherence to MI treatment guidelines was recently shown to improve survival among patients in a Swedish registry who survived a first ST-segment elevation MI (STEMI).⁵ During the 12-year study period between 1996 and 2007, the use of antiplatelet agents, β -blockers, statins, and ACE inhibitors or angiotensin II

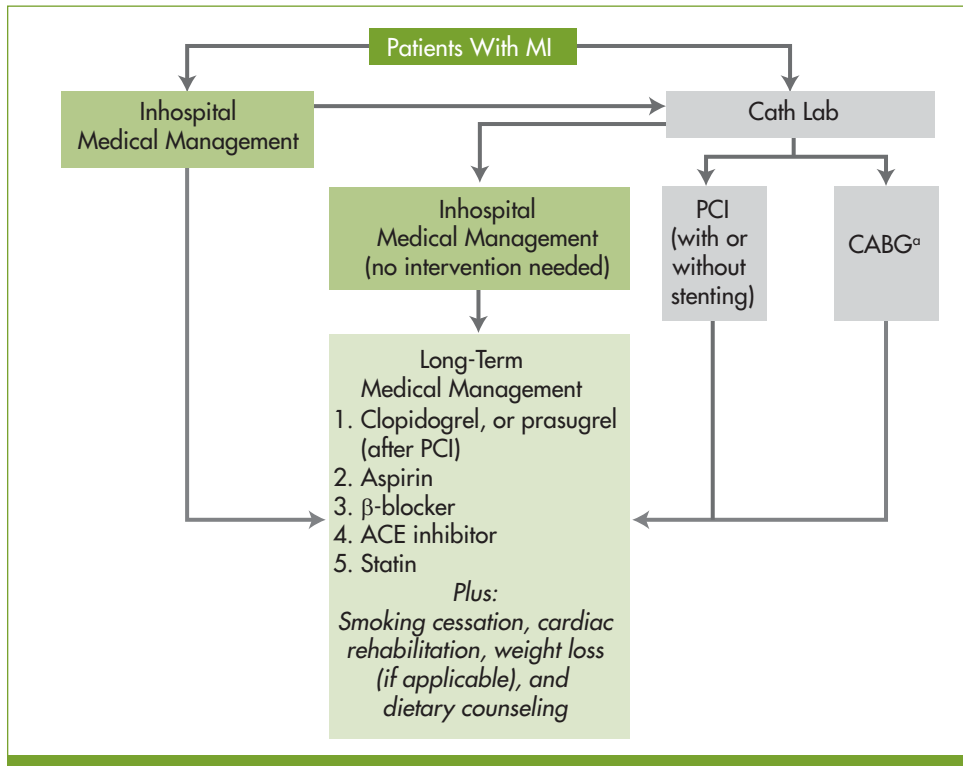


Figure 1. ACC/AHA guidelines recommend dual antiplatelet therapy, β -blockade, ACE inhibition, and statin therapy for long-term management of patients with MI.^{2,4} Barring contraindications in individual patients, this basic strategy is used for secondary prevention regardless of the intervention used to manage the acute event. In addition, cardiac rehabilitation and lifestyle changes to modify risk factors should not be overlooked.

^aIf possible, clopidogrel should be withheld for 5 to 7 days prior to the procedure. ACC = American College of Cardiology; ACE = angiotensin-converting enzyme; AHA = American Heart Association; CABG = coronary artery bypass grafting; PCI = percutaneous coronary intervention.

receptor blockers all increased, and this adoption of evidence-based treatments was associated with decreases in in-hospital mortality as well as mortality 30 days immediately following the event and 1 year after hospital discharge (Figure 2).⁵

Dual Antiplatelet Therapy Is Essential

Because of the key role of platelets in the pathophysiology of atherosclerosis, AHA/ACC guidelines recommend dual antiplatelet therapy with aspirin (a thromboxane inhibitor) and either clopidogrel or prasugrel (each a thienopyridine P2Y₁₂ adenosine diphosphate receptor antagonist) as an essential component of postdischarge care for patients with MI (Table 1).^{2,4} The optimal daily dose of aspirin ranges from 75 mg to 325 mg. Based on data from a meta-analysis of 65 randomized trials in high-risk (including post-MI) patients, aspirin doses in this range reduced the odds of a vascular event (including nonfatal MI, nonfatal stroke, and death from vascular causes) 26% to 32%, compared with controls, with no observed dose response.⁸ The AHA/ACC guidelines recommend that aspirin therapy be continued indefinitely.^{2,4}

When combined with aspirin, both clopidogrel and prasugrel have been shown to significantly decrease the risk of cardiac events and death in patients with non-ST-segment elevation MI (NSTEMI) or STEMI.^{2,4} Prasugrel's Food and Drug Administration (FDA)-approved use for patients with MI is limited to patients who have been managed with percutaneous coronary intervention (PCI).⁹ The relative efficacy of clopidogrel and prasugrel for secondary prevention was established in the Trial to Assess Improvement in Therapeutic Outcomes by Optimizing Platelet Inhibition with Prasugrel-Thrombolysis in Myocardial Infarction 38 (TRITON-TIMI 38) trial.¹⁰ Patients with unstable angina (UA), NSTEMI, or STEMI scheduled for PCI (N = 13,608) were randomized to maintenance treatment with either prasugrel 10 mg/d or clopidogrel 75 mg/d. Compared with clopidogrel, prasugrel achieved significantly greater reductions in the rates of CV death and nonfatal MI or stroke (12.1% vs 9.9%; $P < .001$) and stent thrombosis (2.4% vs 1.1%; $P < .001$).¹⁰ However, this increase in efficacy was accompanied by small but significantly higher rates of bleeding, including major bleeding (2.4% vs 1.8%, $P = .03$), life-threatening bleeding (1.4% vs 0.9%, $P = .01$), and fatal bleeding (0.4% vs 0.1%, $P = .002$).

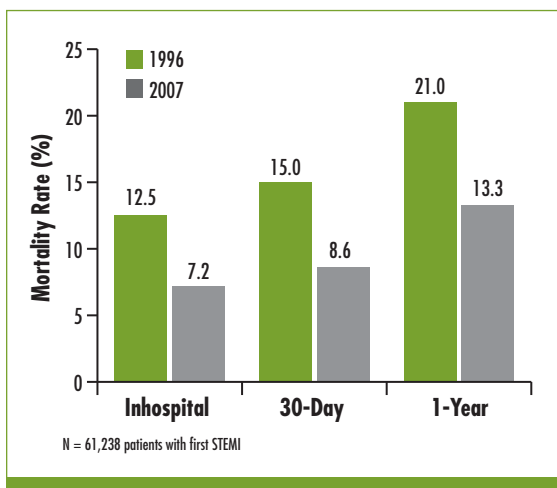


Figure 2. Adherence to evidence-based treatment guidelines decreases short- and long-term mortality after MI.⁵ During the study period between 1996 and 2007, use of aspirin, clopidogrel, β -blockers, statins, and ACE inhibitors or angiotensin II receptor blockers all increased among patients in a Swedish registry who survived a first STEMI (N = 61,238). This increased use of evidence-based treatments was associated with significant reductions in the rates of in-hospital mortality ($P < .001$), 30-day mortality ($P < .001$), and 1-year mortality ($P < .001$).

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Table 1.

Dual Antiplatelet Therapy for Secondary Prevention: ACC/AHA Recommendations^{2,4}

Agent	Daily Dose	Duration
NSTEMI Managed Medically		
Aspirin, <i>plus</i>	75-162 mg	Indefinitely
Clopidogrel	75 mg	At least 1 month and ideally up to 1 year
NSTEMI or STEMI Managed With PCI and Stenting		
Aspirin, ^a <i>plus</i>	162-325 mg	At least 1 month (BMS) or 3-6 months (DES)
	75-162 mg	Indefinitely
Clopidogrel, ^b <i>or</i>	75 mg	At least 12 months
Prasugrel ^{b,c}	10 mg	At least 12 months

^aThe lower dose may be used initially if the patient is considered to be at high risk of bleeding.

^bContinuation of treatment beyond 15 months may be considered for patients who underwent DES implantation.

^cDosing with 5 mg/d may be considered in patients with a body weight <60 kg; prasugrel is contraindicated in patients with active pathologic bleeding or a history of TIA or stroke and generally should not be used in patients aged ≥75 years unless they are at high risk of a recurrent event (eg, because of diabetes or other risk factors).

BMS = bare metal stent.

In a subgroup analysis, patients with a previous stroke or transient ischemic attack (TIA), patients ≥75 years of age, and patients weighing less than 60 kg were identified as having an increased risk of bleeding and decreased net clinical benefit with prasugrel versus clopidogrel.¹⁰ Thus, prasugrel is contraindicated in patients with active pathologic bleeding or history of TIA or stroke and generally is not recommended in patients ≥75 years of age unless they are at high risk for a recurrent event (eg, because of diabetes). Prasugrel therapy also should not be started in patients likely to undergo urgent CABG surgery.⁹

Multiple Interventions Are Needed

In addition to dual antiplatelet therapy, ACC/AHA guidelines recommend β-blockers for cardioprotection for all patients after an MI unless contraindicated, and inhibition of the renin-angiotensin-aldosterone system (eg, with an ACE inhibitor). Patients with hyperlipidemia should receive statin therapy to decrease low-density lipoprotein cholesterol (LDL-C) levels to a target of at least <100 mg/dL and potentially <70 mg/dL. Patients with blood pressure levels >140/90 mm Hg (or >130/80 mm Hg in patients with kidney disease or diabetes) should receive appropriate antihypertensive medication.²

Nonpharmacologic interventions also should not be overlooked. The ACC/AHA guidelines recommend clinicians educate patients about smoking cessation, weight reduction (when applicable), and dietary changes and refer them for cardiac rehabilitation when appropriate.^{2,3} Lifestyle changes can be difficult to effect in patients. Experiencing an MI often motivates patients to make the needed modifications, and clinicians should provide reinforcement at each office visit.^{2,3}

Treatment Adherence Issues

Postdischarge Delays Increase Risk Early

Ensuring that patients with MI begin their dual antiplatelet regimen immediately after hospital discharge is critical. In a recent retrospective cohort study of patients (N = 7402) discharged from the hospital after implantation of a drug-eluting stent (DES), 16.3% (n = 1210) delayed filling their prescriptions for clopidogrel, and 13.6% of the patients who delayed (n = 165) never filled the prescription.¹¹ Any delay, compared with filling the prescription on the day of discharge, was associated with higher rates of adverse outcomes. This association persisted regardless of delay duration and adjustments for delays in filling other medications (Figure 3). In multivariate analysis, any delay in filling clopidogrel prescriptions significantly increased the risk of death or MI (hazard ratio [HR], 1.54; 95% confidence interval [CI], 1.24-1.91) as well as the risk of death alone (HR, 1.45; 95% CI, 1.06-1.97). Most adverse events occurred early, within 30 days of hospital discharge, which emphasizes the importance of the transition period from inpatient to outpatient care.¹¹

Similar findings regarding the impact of treatment adherence on mortality risk were observed in a population-based cohort study of patients from an acute MI registry in Canada

(N = 4591).⁶ A total of 12,832 discharge prescriptions were written and tracked through the Ontario Drug Benefit prescription claims database. Only 74% of patients filled all prescriptions within 120 days after hospital discharge. The lowest rates of prescription fills for cardiac medications within this timeframe were for antiplatelet therapies (55.7%); in contrast, >90% of patients filled prescriptions for ACE inhibitors (96.2%), statins (94.8%), and β -blockers (92.0%). The 1-year mortality rates increased with primary nonadherence: 12.8% among patients who filled all prescriptions, 20.5% among those who filled some, and 30.4% among those who filled none.⁶

Long-Term Adherence Is Poor

Adherence to antiplatelet therapies over the long term is poor. Up to 18% of patients with angiographically documented coronary artery disease (CAD) stop aspirin therapy after 1 year.¹² Among patients from the Prospective Registry Evaluating Myocardial Infarction: Events and Recovery (PREMIER) who received DES implantation (N = 500), 1 in 7 (13.6%) stopped thienopyridine therapy within 30 days of hospital discharge. Those who discontinued therapy were more likely to be older or unmarried, not have a high school diploma, avoid care because of its cost, or have pre-existing CV disease or anemia. Importantly, a higher rate of discontinuation also was seen in patients who did not receive instructions about discharge therapy or a cardiac rehabilitation referral.¹³

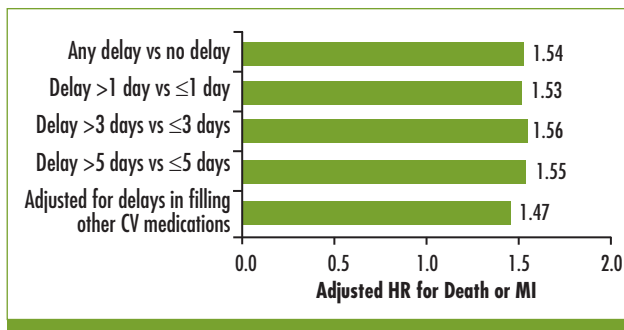


Figure 3. Any delay in filling clopidogrel prescriptions after hospital discharge increases the risk of death or MI.¹¹ Among 7410 patients discharged after DES implantation, 1 in 6 delayed filling their initial clopidogrel prescription. The cumulative incidence of death or MI almost doubled among those patients who delayed filling the prescription (14.3% vs 7.9%; $P < .001$).

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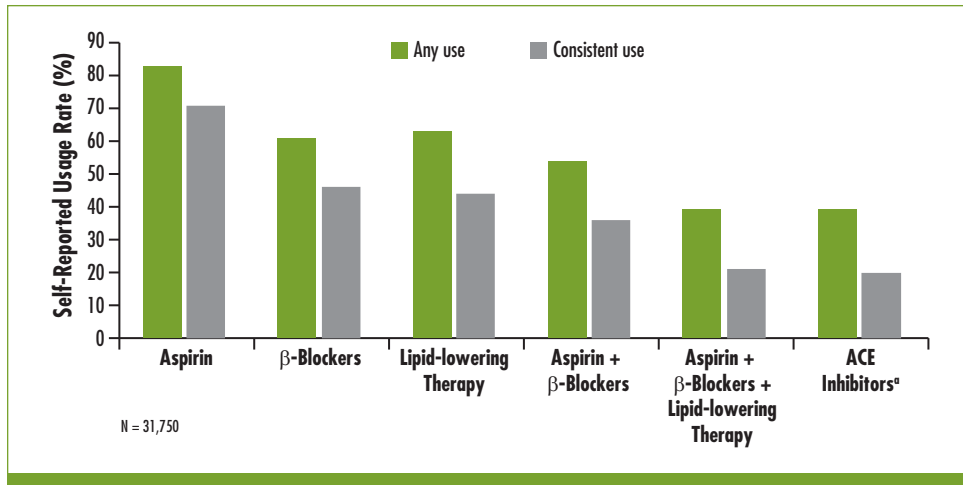


Figure 4. Rates for consistent use of evidence-based secondary prevention therapies for CAD are low.⁷ Among patients with CAD from the Duke Databank for Cardiovascular Disease (N = 31,750), 71% reported using aspirin consistently; however, less than half reported consistent usage of other treatments or treatment combinations.

^aValues for ACE inhibitor usage are for CAD patients without heart failure (n = 22,539).

Self-reported use—especially consistent use—of other secondary prevention therapies for CAD may be even lower. An analysis of treatment usage rates among patients with CAD from the Duke Databank for Cardiovascular Disease (N = 31,750) found only aspirin was used consistently in >50% of patients (Figure 4).⁷ In addition, data show that statin use declines early, particularly in patients who are asymptomatic. Within 6 months after treatment initiation, statins are discontinued by approximately half of the patients, and adherence continues to decline over time.¹⁴

Nonadherence Increases Adverse Event Risk

The risk of adverse coronary events increases with treatment nonadherence or premature discontinuation. A meta-analysis of 6 studies of patients with or at risk for CAD (N = 50,279) found a 3-fold increased risk for major adverse cardiac events with aspirin discontinuation or nonadherence (odds ratio [OR], 3.14; 95% CI, 1.75-5.61; *P* = .0001). The average time between aspirin withdrawal and a thrombotic event was 10.66 days (95% CI, 10.25-11.07). In the subgroup of patients with acute coronary syndrome (ACS), discontinuation or nonadherence to aspirin doubled the risk of death and/or MI (OR, 1.82; 95% CI, 1.52-2.18).¹⁵ Similar findings were seen in a recent analysis of primary care patients in the United Kingdom with a first prescription for aspirin for secondary prevention of CV events (N = 39,513). Compared with current aspirin users, patients with known CAD who stopped aspirin had a 60% increased risk of nonfatal MI alone (rate ratio 1.63; 95% CI, 1.23-2.14) and a 40% increased risk of nonfatal MI or death from coronary heart disease (rate ratio 1.43; 95% CI, 1.12-1.84). Half of all patients were nonadherent to aspirin therapy after a few years.¹⁶

The risks for adverse outcomes associated with nonadherence or premature discontinuation of antiplatelet therapy persist over the long term. The all-cause mortality rate 12 months after MI was 7.5% among patients in the PREMIER study who discontinued thienopyridine therapy within 30 days of hospital discharge, compared with 0.7% among those who continued taking thienopyridines ($P < .0001$).¹³ This translated into an HR of 9.02 (95% CI, 1.3-60.6; $P = .02$). The rates of rehospitalization for cardiac events within 12 months also were higher among patients who discontinued therapy than among those who continued therapy (23% vs 14%; $P = .08$).¹³ Over 7 years, a 72% increase in all-cause mortality risk has been associated with nonadherence to aspirin therapy (HR, 1.72; 95% CI, 1.54-2.38).¹⁵

The long-term hazards of nonadherence are not limited to antiplatelet therapies. In a retrospective study of 15,767 patients with CAD and a median follow-up of 4.1 years, nonadherence to β -blockers, statins, and/or ACE inhibitors was associated with a 10% to 40% relative increase in CV hospitalization risk and 50% to 80% relative increase in mortality risk.¹⁷ These findings reinforce the need to address the issue of treatment nonadherence to improve patient outcomes.

Adherence Improvement Strategies

Clinicians and patients often have different perspectives on the reasons underlying premature treatment discontinuation. In one study, patients with MI who had undergone DES implantation ($n = 22$) were interviewed about reasons for discontinuing prescribed antiplatelet therapy (clopidogrel). Clinicians ($n = 17$) who were not the care providers of the patients interviewed also were asked about their experience with treatment discontinuation. Both groups identified problems with transition of care; however, the clinicians cited system-level factors (ie, cost of clopidogrel and poor transitions of care—especially from the inpatient to the outpatient setting), and patients focused on the breakdown of direct communications (ie, lack of knowledge about the duration and purpose of treatment and poor patient-clinician or clinician-clinician communications).¹⁸ These data underscore the importance of clinician-patient communication and the need for ongoing education to ensure patients understand the importance of their secondary prevention regimen and the risks of nonadherence.

Because the risk of stent thrombosis increases dramatically with the premature discontinuation of dual antiplatelet therapy, the ACC and AHA have issued a science advisory with strategies for preventing nonadherence (Table 2).¹⁹ Clinicians should evaluate the likelihood of their patients adhering to 12 months of thienopyridine therapy prior to DES placement and consider an alternative management approach if the risk of poor adherence is high. Clinicians must also stress the importance of patients contacting them before discontinuing antiplatelet therapy—even if they are told to do so by another healthcare provider as preparation for a procedure or surgery. The risks of periprocedural bleeding should be weighed carefully against the risks of thrombosis.¹⁹

Treatment Optimization

When patients experience a recurrent event despite good adherence to their prescribed regimen for secondary prevention of MI, clinicians should consider the possibility of drug-drug interactions or drug resistance.

1 in 4 Patients May Be Aspirin-Resistant

A meta-analysis of 20 studies comprising 2930 patients found aspirin resistance in 28% ($n = 810$).²⁰ Men were significantly less likely to be aspirin-resistant than women ($P < .001$), and patients

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Table 2.

Strategies for Preventing Premature Discontinuation of Antiplatelet Therapy: ACC/AHA Recommendations¹⁹

Before stent implantation
<ul style="list-style-type: none">➤ Discuss with your patients the need for dual antiplatelet therapy➤ Consider avoiding DES placement if a patient is unlikely to adhere to 12 months of thienopyridine therapy
Before hospital discharge
<ul style="list-style-type: none">➤ Educate your patients about the reasons for thienopyridine therapy and the significant risks (ie, stent thrombosis, MI, death) associated with premature discontinuation➤ Instruct patients to contact you <i>before</i> stopping any antiplatelet therapy—even if they are told to stop by another healthcare provider
Before surgery
<ul style="list-style-type: none">➤ Defer elective surgical procedures that carry a significant risk of perioperative or postoperative bleeding until patients have completed the recommended course of thienopyridine therapy➤ If surgery that mandates discontinuation of thienopyridine therapy cannot be deferred<ul style="list-style-type: none">– Continue aspirin if possible– Restart thienopyridine therapy as soon as possible because of risk of late-stent thrombosis

with renal impairment were significantly more likely to be aspirin-resistant than patients with normal renal function ($P < .03$). All patients with aspirin resistance had a significantly higher risk for adverse outcomes than those with aspirin sensitivity, including CV-related events (OR, 3.85; 95% CI, 3.08–4.80; $P < .001$), ACS (OR, 4.06; 95% CI, 2.96–5.56; $P < .001$), and death (OR, 5.99; 95% CI, 2.28–15.72; $P < .003$). Clinicians should consider the possibility of aspirin resistance in post-MI patients who are adherent to therapy but who experience stent thrombosis or other adverse cardiac events.²⁰

Clopidogrel Resistance May Be Due to Drug Interactions or Genetic Variants

Clopidogrel is metabolized by the cytochrome P450 (CYP450) system of isoenzymes, including CYP2C19, which results in the potential for drug-drug interactions with other agents metabolized via this pathway. Concomitant use of proton pump inhibitors (PPIs) may decrease the antiplatelet effects of clopidogrel.^{21,22} A retrospective cohort study of data from patients with acute MI or UA discharged from Veterans Health Administration hospitals (N = 8205) found that patients taking clopidogrel concomitantly with a PPI (chiefly omeprazole or rabeprazole) had an increased risk of death or rehospitalization for ACS compared with those taking clopidogrel without a PPI (OR, 1.25; 95% CI, 1.11–1.41).²¹ In 2009, the FDA warned that omeprazole use should be avoided by patients receiving clopidogrel because the antiplatelet effect of the drug could be reduced by about 50%; it also advised against the use of esomeprazole.²² However, support for a PPI-clopidogrel interaction across studies varies, and there is no consensus on its clinical significance.^{4,23,24} The only prospective, randomized, controlled trial to date investigating this effect, the Clopidogrel and the

Optimization of Gastrointestinal Events (COGENT) study, found no clinically relevant adverse CV interaction between clopidogrel and omeprazole.²⁵ This study investigated a fixed-dose combination clopidogrel/omeprazole pill, with different pharmacokinetics than the 2 medications taken separately, and was terminated prematurely, which limited follow-up.²⁵ For clopidogrel-treated patients who need to reduce stomach acid, the FDA recommends ranitidine, famotidine, nizatidine, or antacids—none of which inhibit the CYP2C19 isoenzyme.²²

Because clopidogrel is a prodrug, it must be metabolized to its active form. However, the genes encoding CYP450 isoenzymes involved in clopidogrel's metabolism are polymorphic.²⁶ In 2010, the FDA warned that patients with decreased *CYP2C19* function due to genetic polymorphisms, who account for 2% to 14% of the population, metabolize clopidogrel poorly. As a result, the drug is not effectively converted to its active form, and its antiplatelet effects are reduced.²⁷ TRITON-TIMI 38 trial data were analyzed to determine whether clopidogrel-treated patients with ACS who had reduced-function CYP alleles (carriers) experienced a higher rate of adverse CV outcomes than those who did not have the genetic polymorphisms (noncarriers). Both the risk of death from CV causes, MI, or stroke and the rate of stent thrombosis were significantly higher in the carriers (Figure 5).²⁶

In 2010, the ACC/AHA provided recommendations for clinicians who suspect a patient may have clopidogrel resistance due to genetic polymorphisms.²⁸ Routine genetic or platelet function testing is not advised but may be considered for patients with a moderate or high risk for a poor outcome. A recent analysis indicated that platelet reactivity at 1 month post-PCI in patients taking clopidogrel may provide a more accurate measure of the potential for clopidogrel resistance and poor outcomes than a measurement taken during hospitalization.²⁹ If a patient taking clopidogrel who is treatment-adherent has an adverse CV event, clinicians may increase the maintenance dose of clopidogrel to 150 mg/d, add cilostazol to standard doses of aspirin and clopidogrel, or use cilostazol alone. Follow-up platelet function testing should be considered in patients given cilostazol to ensure adequate platelet inhibition. The ACC/AHA state, however, that the risk/benefit ratios for the safety and efficacy of these therapeutic strategies remain to be determined.²⁸ Alternatively, if contraindications are not present, clinicians can switch the patient to prasugrel, the antiplatelet effects and efficacy of which have not been shown to be impacted by *CYP2C19* polymorphisms.²⁸⁻³⁰

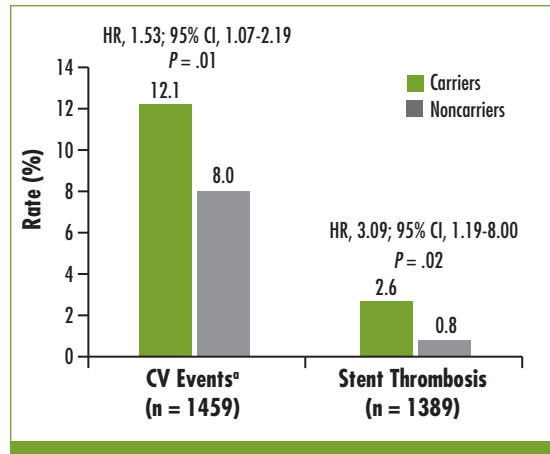


Figure 5. The risk of adverse events during clopidogrel therapy is increased in patients who are poor metabolizers of the drug.²⁶ Among patients with ACS who were treated with clopidogrel, the rates of CV events and stent thrombosis were higher in those who were carriers of a *CYP2C19* reduced-function allele.

^aRisk of death from CV causes, MI, or stroke.

CASE: 58-Year-Old Man Hospitalized With Acute MI



History and Presentation

Jim, age 58 years, has been your patient for 3 years. He has a history of hypertension and dyslipidemia, which have been controlled with amlodipine 5 mg/d and simvastatin 20 mg/d. He admits to being “a little chubby” and has a 30-year history of cigarette smoking (2 packs/d). Jim was admitted to the hospital complaining of chest pain and diagnosed with acute STEMI. He underwent PCI and DES implantation to his left anterior descending coronary artery and is now doing well. The discharge regimen prescribed by Jim’s cardiologist includes aspirin 325 mg/d, clopidogrel 75 mg/d, metoprolol 100 mg/d, ramipril 10 mg/d, and atorvastatin 40 mg/d.

You visit Jim in the hospital. He thanks you for stopping by and says maybe he should have taken his medications regularly and not skipped a few doses. Jim tells you he will send away for a 90-day supply of his new medications, which he should receive in 1 week.

Clinical Decision Point

What is the most important thing for you to do while Jim is waiting for his prescribed medications to arrive by mail?

- Give Jim samples of clopidogrel
- Tell Jim to double up on his simvastatin
- Schedule a follow-up appointment for 10 days
- Refer Jim to a smoking cessation program

Comment

The best answer is give Jim samples of clopidogrel. Patients with MI treated with a DES who delay filling a prescription for antiplatelet therapy have a significantly increased risk for death or MI, with most adverse cardiac events occurring within 30 days of discharge.¹¹

2-Week Postdischarge Follow-Up Visit

Jim says he is feeling fine and has no complaints. He visited his cardiologist 2 days ago, who told him he was doing well and, because he was symptom-free, Jim should come back to see him in 6 months. Jim’s cardiologist faxed you a copy of his laboratory work-up, which showed that his LDL-C level is 65 mg/dL. His blood pressure is 125/82 mm Hg, and other physical findings are unremarkable.

Clinical Decision Point

What should be your next step in managing Jim’s postdischarge care?

- Review Jim’s prescribed medications with him
- Discuss the importance of taking his medications
- Discuss lifestyle modifications with Jim
- All of the above

Comment

The best answer is all of the above. Clinicians should reinforce the importance of treatment adherence at every follow-up visit. Long-term adherence to secondary prevention medications is poor, and Jim has no symptoms, which may make him more likely to stop taking his medications.^{7,14} Treatment discontinuation would greatly increase Jim's risk of an adverse outcome, including stent thrombosis, recurrent MI, or death.^{15,17,19} His recent MI also provides an opportunity to reinforce his need to make appropriate lifestyle changes, including weight reduction and smoking cessation.³

3-Month Postdischarge Follow-Up Visit

Jim says he is doing OK except for heartburn, which he has had for years and which bothers him at night, particularly if he eats late in the evening or eats spicy food. He asks you if the "purple pill" talked about on television is something he could take. Physical findings are unremarkable; his blood pressure is 126/84 mm Hg.

Clinical Decision Point

What should you recommend for managing Jim's gastroesophageal disease symptoms?

- Give Jim a prescription for esomeprazole
- Advise Jim to buy over-the-counter (OTC) omeprazole
- Advise Jim to eat earlier in the evening and avoid spicy food
- Advise Jim to buy OTC ranitidine and to take it at bedtime

Comment

The best answer is advise Jim to buy OTC ranitidine and to take it at bedtime. The FDA recommends against using omeprazole or esomeprazole concomitantly with clopidogrel because these PPIs may decrease the conversion of clopidogrel to its active form via the *CYP2C19* pathway and decrease its antiplatelet effects. Ranitidine, which (like famotidine, nizatidine, and antacids) does not inhibit the *CYP2C19* isoenzyme, would not interfere with clopidogrel's metabolism.²²

6-Month Follow-Up Visit

It has been 7 months since his stent placement, and Jim reports feeling great. He shows you some ecchymoses on his hands and arms, which his cardiologist said were due to the aspirin and clopidogrel. He is feeling so well that he wants to know if he can stop taking some of his pills. His blood pressure is 127/85 mm Hg, and his LDL-C level is 67 mg/dL.

Clinical Decision Point

How should you respond to Jim's concerns?

- Switch Jim to the atorvastatin/amlodipine combination pill
- Offer Jim reassurance and empathy, but stress the importance of treatment adherence
- Stop clopidogrel but continue aspirin
- Stop aspirin but continue clopidogrel

Comment

The best answer is offer Jim reassurance and empathy, but stress the importance of treatment adherence. The ACC and AHA guidelines recommend that aspirin therapy be continued indefinitely and that thienopyridine therapy be continued for at least 12 months after DES placement.^{2,4} While the combination of atorvastatin/amlodipine would eliminate 1 pill, Jim would lose the cardioprotective benefit of inhibiting the renin-angiotensin system since he would no longer be taking the ACE inhibitor.

3 Weeks Later

Jim's cardiologist calls and says Jim was readmitted to the hospital with symptoms of ACS. Cardiac catheterization revealed stent thrombosis. Jim is now doing "OK."

Clinical Decision Point***What might have contributed to Jim's stent thrombosis?***

- Aspirin or clopidogrel resistance
- Poor treatment adherence
- OTC omeprazole that Jim took for his heartburn
- Any of the above

Comment

The best answer is any of the above. Nonadherence/discontinuation of thienopyridine therapy within 1 year of DES placement increases the risk of stent thrombosis.¹⁹ Aspirin resistance may affect more than a quarter of the population.²⁰ Finally, some genetic polymorphisms decrease *CYP2C19* function, and omeprazole inhibits the *CYP2C19* enzyme; either situation could interfere with the metabolism of clopidogrel and decrease its antiplatelet effects.^{22,27}

Clinical Decision Point***What is the best approach to try to prevent another stent thrombosis?***

- Counsel Jim about the need to take all his medications
- Increase his aspirin dose
- Switch him from clopidogrel to prasugrel
- Add warfarin to his regimen

Comment

The best answer is switch him from clopidogrel to prasugrel. For patients with MI who have been prescribed clopidogrel for secondary prevention and are adhering to treatment and who have an adverse cardiac event, the ACC/AHA guidelines recommend clinicians consider alternative therapeutic strategies, including prasugrel.²⁸ It is unlikely that increasing the aspirin dose would provide an added antiplatelet effect, but it would increase the risk of bleeding.⁸ Warfarin is a vitamin K inhibitor and anticoagulant recommended for post-MI patients with a clinical indication such as a left ventricular thrombus or atrial fibrillation; it is not as effective as dual antiplatelet therapy for preventing platelet-dependent stent thrombosis.³

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