Antiplatelet therapy in acute coronary syndromes

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Antiplatelet agents are an essential component of the treatment of acute coronary syndromes (ACS). In numerous clinical trials, aspirin, thienopyridines, and glycoprotein IIb/IIIa inhibitors have been shown to reduce the incidence of ischaemic events in patients with unstable angina, non-ST-elevation myocardial infarction, and ST-elevation myocardial infarction. Aspirin is appropriate for lifelong therapy in patients with ACS. Clopidogrel is recommended for most patients with ACS for short- or long-term therapy, depending on the patient’s level of risk. New antiplatelet agents with distinct pharmacological properties may offer advantages, including faster onset of action, greater potency, and reversibility of effects. The treatment of ACS has evolved considerably in the past decade, with a trend towards greater consistency of care and more widespread provision of evidence-based therapies. Registries and surveys offer opportunities to educate health care providers on compliance with current guideline recommendations for the management of patients with ACS, which should lead to improved clinical outcomes.

Introduction
Thrombosis occurring in the presence of underlying atherosclerosis is a key pathological step in the development of acute coronary syndromes (ACS)—unstable angina (UA), ST-elevation myocardial infarction (STEMI), and non-STEMI (NSTEMI).1 Because platelets play an important role in the development of thrombosis,2 antiplatelet agents are a mainstay of the treatment of ACS. This article will review the recommendations for the use of antiplatelet agents and the evidence demonstrating their contribution to favourable outcomes.

Current use of antiplatelet agents in ST-elevation myocardial infarction

Guideline recommendations
Guidelines from the European Society of Cardiology (ESC)3 and the American College of Cardiology and the American Heart Association (ACC/AHA)4 recommend routine use of aspirin as soon as possible after the onset of symptoms of acute myocardial infarction (MI) and as lifelong therapy thereafter. Clopidogrel is recommended as an alternative in patients who cannot tolerate aspirin.3 Clopidogrel is recommended in addition to aspirin in patients in whom percutaneous coronary intervention (PCI) is planned, for 3–4 weeks after placement of a bare-metal stent (BMS),3 and by the ESC and the US Food and Drug Administration for 12 months after placement of a drug-eluting stent (DES).6,7 The glycoprotein IIb/IIIa inhibitor (GPI) abciximab, with tirofiban and eptifibatide as alternatives, is recommended for patients undergoing PCI, with or without stenting.3,4

Aspirin in patients with ST-elevation myocardial infarction
Lifelong aspirin therapy is appropriate for all patients with STEMI in whom it is not contraindicated. A meta-analysis of trials comprising 19 302 patients with acute MI found that antiplatelet therapy—primarily with aspirin—resulted in an approximately 25% reduction in
serious vascular events with a small risk of bleeding complications. Aspirin doses of 75–100 mg appear to be as effective as higher doses and less likely to cause bleeding.

Thienopyridines in patients with ST-elevation myocardial infarction

As the use of PCI has grown, thienopyridines have come to play an increasingly important role in the treatment of STEMI. Clopidogrel has largely replaced ticlopidine because of its equal efficacy and better safety profile. In a dose of 75 mg/day, clopidogrel is as effective as aspirin at preventing ischaemic events in patients with a history of recent MI, with a similar safety profile. Greater effectiveness can be obtained from combining clopidogrel and aspirin. In the COMMIT trial, the routine addition of clopidogrel 75 mg/day to aspirin therapy for 4 weeks in patients with acute MI resulted in a 9% proportional reduction in death, re-infarction, or stroke (P = 0.002) and a 7% proportional reduction in death (P = 0.03). Even though no loading dose was used, the benefit of clopidogrel therapy was seen almost immediately in an 11% proportional reduction in mortality in the first 2 days after the initiation of therapy (P = 0.019).

Used with fibrinolysis in patients with STEMI, clopidogrel has been shown to reduce the risk of in-hospital arterial occlusion, death, or recurrent MI by 36% (P < 0.001) and the 30-day risk of cardiovascular death, recurrent MI, or urgent revascularization by 20% (P = 0.03), with no significant increase in major bleeding. In patients with STEMI who received fibrinolysis and then underwent PCI, a 300 mg clopidogrel loading dose given before fibrinolysis followed by 75 mg/day until coronary angiography reduced by 46% the 30-day occurrence of the composite endpoint of cardiovascular death, recurrent MI, or stroke; the benefit was similar whether patients underwent PCI urgently or electively and was unrelated to the timing of PCI. The ongoing CIPAMI trial will investigate the administration of clopidogrel as early as possible after the diagnosis of STEMI and compare it with later administration, after initial angiography.

Glycoprotein IIb/IIIa inhibitors in patients with ST-elevation myocardial infarction

A meta-analysis of 11 trials that included 27 115 patients with STEMI showed that abciximab treatment reduced the rate of 30-day re-infarction in all trials combined, in primary angioplasty trials, and in fibrinolysis trials. Overall, abciximab treatment did not result in a reduction in 30-day or 1-year mortality. However, abciximab-treated patients who underwent primary angioplasty did have lower 30-day mortality (2.4% vs. 3.4%; odds ratio [OR] 0.68, 95% confidence interval [CI] 0.47–0.99, P = 0.047) and lower 1-year mortality (4.4% vs. 6.2%; OR 0.69, 95% CI 0.52–0.92, P = 0.01). Abciximab had no effect on mortality when used in patients treated with fibrinolysis.

A more recent meta-analysis pooled long-term data from three trials that included 1101 high-risk patients with STEMI who underwent primary PCI with stenting and were randomized to abciximab or placebo. After up to 3 years of follow-up, the frequency of death or re-infarction was reduced from 19.0% in the placebo group to 12.9% in the abciximab group (relative risk [RR] 0.633, 95% CI 0.452–0.887, P = 0.008). Analysed separately, the rate of re-infarction was significantly reduced by abciximab treatment, and the rate of death nearly so, with no significant increase in bleeding.

Current use of antiplatelet agents in non-ST-elevation-acute coronary syndromes

Guideline recommendations

Because it has been shown to reduce death and MI in patients with UA or NSTEMI and is associated with a low incidence of adverse effects, aspirin is recommended by guidelines as acute and long-term treatment for all patients with NSTE-ACS unless it is contraindicated. Clopidogrel in combination with aspirin, or as monotherapy if aspirin is not tolerated, is similarly recommended for acute treatment at a dose of 300 mg, followed by 12 months of treatment at 75 mg/day. Because of increased risk of surgical bleeding, clopidogrel should be withheld for 5 days before coronary artery bypass grafting (CABG) if clinically feasible. Treatment with eptifibatide or tirofiban in addition to oral antiplatelet therapy is recommended for initial early treatment in patients at intermediate to high risk; in high-risk patients undergoing PCI not pre-treated with a GPI, abciximab is recommended immediately following angiography. Bivalirudin may be considered an alternative to GPs plus unfractionated heparin (UFH)/low-molecular-weight heparin (LMWH).

Aspirin in patients with non-ST-elevation-acute coronary syndromes

Aspirin therapy reduces the risk of MI, ischaemic stroke, and cardiovascular death in patients with NSTE-ACS and is an essential component of therapy for all patients in whom it is not contraindicated. The ideal aspirin dosage is unknown, but 75–150 mg/day is effective, whereas higher doses have not been shown to provide additional benefit and may carry an increased risk of bleeding. The benefits of daily aspirin administration persist for at least 2 years; given its relative safety, there appears to be no reason not to recommend lifelong aspirin therapy.

Clopidogrel in patients with non-ST-elevation-acute coronary syndromes

Like aspirin, clopidogrel has an established role in NSTE-ACS, based, to a large degree, on the results of the CURE trial, which randomized 12 562 patients with NSTE-ACS to receive clopidogrel or placebo.
All patients received aspirin. Clopidogrel was given in a loading dose of 300 mg, followed by 75 mg/day for 3–12 months. The composite of cardiovascular death, non-fatal MI, or stroke occurred significantly less often in the clopidogrel group (9.3 vs. 11.4%, RR 0.80, 95% CI 0.72–0.90, \( P < 0.001 \)) (Figure 1).\(^{20}\) Major bleeding occurred in 3.7% of patients in the clopidogrel group and 2.7% of patients in the placebo group (RR 1.38, 95% CI 1.13–1.67, \( P = 0.001 \)), although the rates of fatal bleeding, bleeding requiring surgical intervention, and haemorrhagic stroke did not differ significantly.\(^{20}\) Among the 2658 patients in the CURE trial who underwent PCI, the incidence of cardiovascular death or MI was reduced by a third in the clopidogrel group.\(^{21}\)

The appropriate dose of clopidogrel before PCI has been the subject of debate. Given its slow onset of action and the variability of patient response to the drug, a 300 mg loading dose may be insufficient. When patients undergoing planned PCI were randomized to loading doses of 300 or 600 mg of clopidogrel, the higher dose was associated with a >50% risk reduction in the 30-day incidence of MI, a difference due entirely to a reduction in peri-procedural MI, with no excess of bleeding.\(^{22}\) A 900 mg loading dose appears to offer no additional advantage.\(^{23}\)

**Glycoprotein IIb/IIIa inhibitors in patients with non-ST-elevation-acute coronary syndromes**

Large trials have examined the use of GPIs in patients with NSTE-ACS whose treatment plan called for medical management. In the GUSTO IV-ACS trial,\(^{24}\) 7800 patients with NSTE-ACS not scheduled for PCI and receiving aspirin and either UFH or LMWH were randomized to an abciximab bolus and 24 h infusion, an abciximab bolus and 48 h infusion, or placebo. The trial found no benefit and an increase in bleeding from abciximab treatment. The PURSUIT trial\(^{25}\) found a significant 1.5% absolute reduction in the 30-day rate of death or non-fatal MI in patients with NSTE-ACS receiving eptifibatide compared with patients receiving placebo (\( P = 0.04 \)); most patients did not undergo PCI. In the PRISM trial,\(^{26}\) 3232 patients with UA already taking aspirin were randomized to receive tirofiban or heparin for 48 h. Tirofiban treatment resulted in a 32% reduction in the composite of death, MI, or refractory ischaemia at 48 h compared with heparin treatment (\( P = 0.01 \)). At 30 days, there was no difference between treatment groups in the occurrence of the composite endpoint, although mortality was lower in the tirofiban group (2.3 vs. 3.6%, \( P = 0.02 \)). Thrombocytopenia occurred significantly more often in the tirofiban group (1.1 vs. 0.4%, \( P = 0.04 \)).

A meta-analysis of six trials that included 31 402 patients with NSTE-ACS for whom an intervention strategy was not planned found a 9% reduction in the risk of death or MI at 30 days in patients given a GPI (10.8 vs. 11.8%, OR 0.91, 95% CI 0.85–0.98, \( P = 0.015 \)).\(^{27}\) The benefit was confined to patients with an elevated troponin level. There was a significantly higher frequency of major bleeding in patients given GPIs (2.4 vs. 1.4%, \( P < 0.0001 \)).

GPIs have been shown to improve outcomes when used in patients undergoing PCI. The ISAR-REACT 2 trial\(^{28}\) randomized 2022 patients undergoing planned PCI to abciximab (0.25 mg/kg bolus followed by 0.125 mg/kg/min infusion for 12 h) plus heparin (70 U/kg) or placebo plus...
heparin (140 U/kg). All patients had been pre-treated with a 600 mg loading dose of clopidogrel and 500 mg of oral or intravenous aspirin. In the abciximab group, there was a 25% reduction in the composite of death, MI, or urgent revascularization within 30 days of randomization (P = 0.03), but the benefit was confined to patients with an elevated troponin level.28

In the ESPRIT trial,29 2064 patients undergoing PCI with stenting were randomized to receive placebo or eptifibatide given as two 180 μg/kg boluses 10 min apart and an infusion of 2.0 μg/kg/min for 18-24 h or until hospital discharge, whichever came first; patients also received aspirin, a thienopyridine, and, at the investigator’s discretion, heparin. At 48 h, the rate of death, MI, urgent target-vessel revascularization, or thrombotic bailout with a GPI was significantly reduced in the eptifibatide group, from 10.5 to 6.6% (P = 0.0015). The 30-day rate of death, MI, or urgent target-vessel revascularization was also significantly reduced in the eptifibatide group, from 10.5 to 6.8% (P = 0.0034).

Tirofiban was compared with abciximab in 4809 patients undergoing elective or urgent PCI with stenting in the TARGET trial.30 All patients received aspirin and, when possible, clopidogrel. At 30 days, the incidence of death, MI, or urgent target-vessel revascularization was significantly lower in the abciximab group (6.0 vs. 7.6%, P = 0.038), primarily due to a lower rate of MI.30 At 1-year follow-up, mortality rates in the two treatment groups were similar.31

Current guidelines recommend administering GPs either ‘upstream’, usually in the emergency department, or later, in the catheterization laboratory.5 In a substudy of the ACUITY trial,32 upstream use of either eptifibatide or tirofiban was compared with the administration of either eptifibatide or abciximab in the catheterization laboratory. Upstream use resulted in a lower rate of ischaemic events but a higher rate of bleeding, such that the net clinical benefit was similar for the two strategies.32 The ongoing EARLY ACS trial33 will compare placebo treatment with the administration of eptifibatide ~25 h before catheterization, allowing provisional use of eptifibatide in the catheterization laboratory, in 10,500 patients with UA or NSTE-ACS undergoing an early invasive treatment strategy.

**Antiplatelet agents in patients receiving stents**

Controversy has surrounded the use of DES since reports of subacute stent thrombosis, manifesting as sudden death or acute MI, appeared soon after their approval. Late stent thrombosis appeared to be associated with the implantation of DES in complex lesions and in patients with complicating conditions such as renal dysfunction or diabetes, not with approved uses, and with premature withdrawal of antiplatelet agents.44 A recent meta-analysis found that the long-term incidence of the combination of death and Q-wave MI is 16–38% higher in patients who receive DES than in patients who receive BMS,35 although another meta-analysis of 14 trials found that patients who received sirolimus-eluting stents had the same risk of stent thrombosis, death, or MI as patients who received BMS but required re-intervention less often.36

Clopidogrel therapy for 6–12 months in addition to lifelong aspirin has been the standard of care in patients receiving DES.5 An observational study found that, for patients who were event-free at 6 or 12 months after implantation of a DES, clopidogrel therapy was a significant predictor of lower risk for death or MI at 24 months; clopidogrel therapy had no such predictive effect in patients who received BMS.37 In contrast, discontinuation of clopidogrel therapy within 30 days after implantation of a DES has been shown to increase the 1-year mortality rate to 7.5% from the 0.7% found in patients who continued clopidogrel therapy (P < 0.0001).38 On the basis of these data, recommendations have been made that clopidogrel therapy be continued for up to 12 months after stent implantation in patients not at high risk for bleeding.6,7

A recent meta-regression of seven trials that randomized a total of 3382 patients receiving stents to clopidogrel or ticlopidine focused on the effects on death or non-fatal MI of a clopidogrel-loading dose.39 Overall, the two drugs were equally effective, but clopidogrel was found to be superior to ticlopidine in the five trials in which a 300 or 600 mg clopidogrel loading dose was used and inferior to ticlopidine in the two studies in which a loading dose was not used.

**New antiplatelet agents**

Despite high clopidogrel loading doses and concomitant use of aspirin, ischaemic events continue to occur. For maximum benefit, clopidogrel should be given at least 6 h before PCI40; it may contribute to bleeding complications in patients who undergo CABG within 5 days of its administration,41 and there is significant variability in patient response.42 These limitations have led to a search for alternative antiplatelet agents.

**Prasugrel**

Prasugrel is a new thienopyridine that has been shown to be more potent than clopidogrel in pre-clinical studies, with a lower rate of non-responders43 and a faster onset of action.44 In the TRITON-TIMI 38 trial, 13 608 moderate- to high-risk patients with NSTE-ACS or STEMI undergoing PCI were randomized to receive prasugrel (60-mg loading dose followed by 10 mg/day) or clopidogrel (300-mg loading dose followed by 75 mg/day) for 6 to 15 months.45 The composite end point of death from cardiovascular causes, nonfatal MI, or nonfatal stroke occurred in 12.1% of patients randomized to clopidogrel and 9.9% of patients randomized to prasugrel (hazard ratio [HR] 0.81, 95% CI 0.73–0.90, P < 0.001). There were also significant reductions in the rates of MI, urgent target-vessel revascularization, and stent thrombosis among patients randomized to prasugrel. The rate of major bleeding was higher in the prasugrel group (2.4 vs. 1.8%, HR 1.32, 95% CI 1.03–1.68, P = 0.03), as were the rates of life-threatening bleeding (1.4 vs. 0.9%,
and more rapid return to baseline platelet function. and trends towards less prolongation of bleeding time during inhibition of platelet aggregation as abciximab treatment. Cangrelor treatment resulted in similar levels of adverse cardiac events was seen in either part of the study. (0.25 mg/kg bolus followed by 0.125 μg/kg/min). No significant difference in major or minor bleeding or in major or minor bleeding events was recorded.

Cangrelor
Cangrelor is an intravenous P2Y12 antagonist that was studied in a phase II safety trial of patients undergoing PCI. In the first part of the randomized, open-label study, three doses (1, 2, or 4 μg/kg/min) of cangrelor were given with aspirin and heparin for 18–24 h beginning before PCI; in the second part of the study, the 4 μg/kg/min dose of cangrelor was compared with abciximab (0.25 mg/kg bolus followed by 0.125 μg/kg/min). No significant difference in major or minor bleeding or in major or minor bleeding events was seen in either part of the study. Cangrelor treatment resulted in similar levels of inhibition of platelet aggregation as abciximab treatment and trends towards less prolongation of bleeding time and more rapid return to baseline platelet function.

Evolving patterns of treatment of acute coronary syndromes
Given that many questions and controversies surround the treatment of ACS, it comes as no surprise that it has undergone considerable change in recent years. Evidence from registries provides a real-world picture of how clinicians approach patients with ACS and where educational efforts should be directed to improve the care of such patients.

Euro Heart Survey on acute coronary syndromes
Within the Euro Heart Survey (EHS) Programme of the ESC, two ACS surveys (ACS I and II) collected data in Europe and the Mediterranean Basin in 2000–2001 and in 2004, and the ESC-ACS registry will continue to do so until November 2008. EHS-ACS I collected data on 10 484 patients in 25 countries, and EHS-ACS II collected data on 6385 patients in 32 countries. The proportion of patients with ST-elevation ACS rose from 42% in EHS-ACS I to 47% in EHS-ACS II, and the proportion of patients with a history of MI fell. The use of coronary angiography, PCI, and intra-coronary stents all increased in EHS-ACS II. Among patients with ST-elevation, the use of PCI increased from 40.4 to 57.8% and the use of stents increased from 31.0 to 52.4%, whereas the use of fibrinolysis declined. Among patients without ST-elevation, the use of PCI increased from 25.4 to 37.1% and the use of stents increased from 18.1 to 33.8%.

More patients received guideline-recommended medications in EHS-ACS II than in EHS-ACS I. The most striking change was in the use of thienopyridines, which increased from 36.1 to 69.8% in patients with ST-elevation and from 27.6 to 67.4% in patients without ST-elevation. There was also a significant increase in the use of statin agents. The use of aspirin, GPIs, angiotensin-converting enzyme (ACE) inhibitors/angiotensin receptor blockers, and beta-blockers all increased, whereas the use of heparins declined.

Presumably as a result of these improvements in therapy, there was a significant decline in mortality rates from EHS-ACS I to EHS-ACS II. In-hospital mortality occurred in 4.9% of EHS-ACS I patients and 4.0% of EHS-ACS II patients (adjusted OR 0.86, 95% CI 0.73–1.01, P = 0.07). Thirty-day mortality occurred in 6.2% of EHS-ACS I patients and 5.1% of EHS-ACS II patients (adjusted OR 0.85, 95% CI 0.73–0.99, P = 0.04).

ACOS registry
The ACOS registry gathered data from 16 817 patients treated in Germany at facilities with intensive care units and offering early reperfusion therapy. An analysis of ACOS patients with STEMI demonstrated the benefit of clopidogrel therapy. One-year mortality was lower in STEMI patients treated with clopidogrel than in those not treated with clopidogrel (3.7 vs. 12.4%, OR 0.27, 95% CI 0.22–0.33, P < 0.001) whether they underwent fibrinolysis, primary PCI, or no reperfusion.

GRACE registry
The GRACE registry has continuously collected data on patients with ACS since 1999. Comparison of 6-month periods during 1999 and 2005 showed that use of PCI increased from 32.4 to 63.5% among patients with STEMI and from 16.9 to 34.6% among patients with NSTE-ACS. Use of guideline-recommended medications, including aspirin, beta-blockers, statins, ACE-inhibitors or angiotensin-receptor blockers, LMWH, thienopyridines, and GPIs, significantly increased. Figure 2 displays this improved adherence to guideline-recommended therapies in patients with NSTE-ACS.

Greater adherence to guidelines was paralleled by improved outcomes. Among STEMI patients, the in-hospital rate of death declined by 3.9 percentage points, congestive heart failure (CHF) or pulmonary oedema declined by 9.0 percentage points, MI > 24 h after presentation or recurrent MI declined by 1.6 percentage points, and cardiogenic shock declined by 2.4 percentage points. At 6 months, the rates of stroke and MI, but not of death, had declined significantly.

Among patients with NSTE-ACS, the in-hospital rate of death declined by 0.7 percentage points, CHF or pulmonary oedema declined by 6.5 percentage points, MI > 24 h after presentation or recurrent MI declined by 1.3
percentage points, and cardiogenic shock declined by 0.2 percentage points. At 6 months, the rates of death and stroke had declined significantly (Table 1).49

**CRUSADE registry**

In the US, the benefits of guideline-recommended therapies for NSTE-ACS have been documented in the CRUSADE initiative, which collected data from 501 hospitals.50 Analysis of the records of 113 595 patients showed that, during the 4 years following the release of the ACC/AHA guidelines,4 adherence to class I recommendations for the use of drug therapy improved; there were steady increases in the use of antiplatelet agents, beta-blockers, clopidogrel, heparin, and GPIs, both in-hospital and at discharge. The proportion of patients who

![Figure 2](image-url)

**Table 1** Changes in clinical outcomes in 27 558 patients with non-ST-elevation-acute coronary syndromes included in the GRACE registry49

<table>
<thead>
<tr>
<th></th>
<th>Number/total (%) of patients</th>
<th>% difference in rates (95% CI)</th>
<th>P-value for linear trendsa</th>
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<tbody>
<tr>
<td><strong>In-hospital outcomesb</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Death</td>
<td>2213 (2.9)</td>
<td>1566 (2.2)</td>
<td>−0.7 (−1.7 to 0.3)</td>
</tr>
<tr>
<td>CHF or pulmonary oedema</td>
<td>2228 (13)</td>
<td>1564 (6.1)</td>
<td>−6.5 (−8.4 to −4.7)</td>
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<tr>
<td>MI &gt;24 h after presentation or</td>
<td>696 (3.0)</td>
<td>1556 (1.7)</td>
<td>−1.3 (−2.7 to 0.1)</td>
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<tr>
<td>recurrent MIc</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Cardiogenic shock</td>
<td>2230 (2.1)</td>
<td>1565 (1.8)</td>
<td>−0.2 (−1.1 to 0.7)</td>
</tr>
<tr>
<td>Stroke</td>
<td>2227 (0.2)</td>
<td>1559 (0.6)</td>
<td>0.3 (−0.1 to 0.7)</td>
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<tr>
<td><strong>Six-month outcomesb</strong></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Death</td>
<td>1942 (4.9)</td>
<td>998 (3.3)</td>
<td>−1.6 (−3.0 to −0.1)</td>
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<tr>
<td>MIc</td>
<td>1901 (1.4)</td>
<td>957 (0.7)</td>
<td>−0.7 (−1.4 to 0.1)</td>
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<tr>
<td><strong>MIc</strong></td>
<td>2.5</td>
<td>2.9</td>
<td>0.4 (−1.7 to 2.5)</td>
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aDouble-sided Cochran–Armitage test or logistic regression using data for all time periods.

bRisk adjustment was applied as the risk profile increased over time.

cFirst time period was for July–December 2002.
received all guideline-recommended medications increased from 30 to 48% for in-hospital medications and from 30 to 50% for discharge medications.50 The use of PCI increased by 8%; however, the increase was greater in low-risk than in high-risk patients.51 After risk adjustment, every 10% increase in adherence to guidelines was associated with a 10% decrease in in-hospital mortality.52

Conclusion
The improved outcomes now being obtained in patients with ACS can be attributed to the publication of comprehensive, authoritative guidelines recommending evidence-based therapies. Important among these recommendations are those pertaining to the short- and long-term use of antiplatelet agents, which have been shown to significantly reduce mortality and ischemic events in patients with UA, NSTEMI, and STEMI. New antiplatelet agents that may provide greater potency, faster onset of action, and less variability in patient response will soon be available.

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References


