Medication Errors in Acute Cardiovascular and Stroke Patients

A Scientific Statement From the American Heart Association

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Medical errors are the eighth leading cause of death in the United States and are estimated to account for somewhere between 44 000 and 98 000 deaths in the United States each year.[1] An exact number of deaths remains both uncertain and controversial, with arguments that the actual figure may be lower[2] or higher.[3] Each year in the United States, the estimated 450 000 preventable medication-related adverse events cost $3.5 billion.[4] In the Health Grades Inc Patient Safety in American Hospitals study, which examined 37 million patient records, it was estimated that 195 000 Medicare patients die due to preventable, in-hospital medical errors annually.[3] Medication errors are the most common type of medical error, and cardiovascular medications prescribed to inpatients account for a large proportion of these errors. An average of 1 medication error occurs per hospitalized patient per day, and one quarter of all medication-related injuries are preventable. The emergency department (ED) and acute hospital setting remain locations at high risk for medication errors.

Since the Institute of Medicine's 2000 report, "To Err Is Human: Building a Safer Health System," there has been heightened awareness of medical and medication errors.[1] In 2001, Congress appropriated $50 million for major initiatives in patient safety and directed the Agency for Healthcare Research and Quality to establish the Center for Quality Improvement and Patient Safety. The following year, the American Heart Association (AHA) issued its first scientific statement on medication errors in acute cardiac care.[5] In 2003, Congress passed the Medicine Modernization Act to charge the Institute of Medicine with formulating a national agenda aimed at reducing medication errors. In these early years after the Institute of Medicine's report, the topic of patient safety became a frequent focus for healthcare leaders, journalists, and concerned citizens. Although significant advances have occurred regarding an understanding of the science and systems involved in medication errors, the building of a culture of safety has proved to be an immense task. Despite this public awareness and the research directed at the problem of medical errors, the impact of medication errors on patient safety remains a significant problem. The Institute of Medicine's update in 2006, entitled "Preventing Medication Errors," makes clear that medication errors still are a serious patient safety concern.[4] The present statement will examine common and serious medication

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errors in acute cardiovascular medicine, with a focus on strategies to reduce medication error frequency and consequences.

The writing group was charged with the task of performing an assessment of the evidence and giving a classification of recommendations and a level of evidence to each recommendation. The American College of Cardiology (ACC)/AHA classification system was used as follows:

Classification of Recommendations

Class I: Conditions for which there is evidence and/or general agreement that a given procedure or treatment is beneficial, useful, and effective.

Class II: Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment.

- **Class IIa:** Weight of evidence/opinion is in favor of usefulness/efficacy.
- **Class IIb:** Usefulness/efficacy is less well established by evidence/opinion.

Class III: Conditions for which there is evidence and/or general agreement that a procedure/treatment is not useful/effective and in some cases may be harmful.

Level of Evidence

Level of Evidence A: Data derived from multiple randomized clinical trials or meta-analyses.

Level of Evidence B: Data derived from a single randomized trial or nonrandomized studies.

Level of Evidence C: Only consensus opinion of experts, cases studies, or standard of care.

For the practice recommendations provided in this statement, the classification of recommendations and the level of evidence determinations were taken from data available from clinical trials or registries about the usefulness/efficacy in different subpopulations. A recommendation with level of evidence B or C does not imply that the recommendation is weak. Many important clinical questions addressed in the guidelines do not lend themselves to clinical trials. Although randomized trials may not be available, there may be a very clear clinical consensus that a particular test or therapy is useful or effective. In 2003, the ACC/AHA Task Force on Practice Guidelines developed a list of suggested phrases to use when writing recommendations. All guideline recommendations have been written in full sentences that express a complete thought, such that a recommendation, even if separated and presented apart from the rest of the document (including headings above sets of recommendations), would still convey the full intent of the recommendation. It is hoped that this will increase readers' comprehension of the guidelines and allow queries at the individual recommendation level.

Medication Error Definition and Categories

A medication error may be defined broadly as events ". . . related to professional practice, healthcare products, procedures, and systems, including prescribing; order communication; product labeling, packaging, and nomenclature; compounding; dispensing; distribution; administration; education; monitoring; and use."[6] This definition is used by the US Pharmacopeia, the US Food and Drug Administration (FDA), and the Centers for Medicare and Medicaid Services. Variations in definitions and abilities to uncover errors have contributed to a wide range in estimates of medication error rates. In the present statement, medication errors will include the following: Improper dosing or timing, delivery of an incorrect or unnecessary medication, administration to the wrong patient (errors of commission), and failure to prescribe appropriate medication therapy or needed monitoring of medication therapy (errors of omission).

Medication Type Errors

To understand and successfully address the problem of medication errors, universal and standardized reporting mechanisms are essential. The US Pharmacopeia's MEDMARX is an anonymous, Internet-accessible program used nationwide by hospitals and related institutions to report, track, and analyze medication errors. In the MEDMARX 2006 report, similar medication names increased the rate of medication errors. As shown in Table 1, errors were higher among the more than 26 000 records with look-alike and/or sound-alike medication names than among other categories.[7] In addition to confusion regarding the medication name, there may be errors related to the selection of an incorrect medication formulation. For example, several antihypertensive and antianginal medications frequently come in various formulations for immediate versus sustained release, including nifedipine, diltiazem, verapamil, metoprolol, carvedilol, and nitrates. In addition, it has become increasingly recognized that acute administration of specific medications may cause QT-interval prolongation, which leads to an increased risk of torsade de pointes.[8] Failure to appropriately monitor the QT interval and adjust therapy in patients receiving QT-prolonging medications constitutes a medication error.

Medication Dosing, Dispensing, and Timing Errors

Anticoagulants, narcotics, and insulins are high-alert medications identified by the Institute for Healthcare Improvement and the Institute for Safe Medication Practices.[9] The Joint Commission describes high-alert medications as those that have the highest risk of causing injury when misused. Medications in this class are most likely to cause significant harm to the patient, even if used as intended. Although mistakes may not be more common in the use of these medications, when errors occur, the impact to the patient may be significant. Other investigators have also identified anticoagulants and antiplatelet agents, commonly used in acute cardiovascular disease management, as among the medication groups that account for the majority of medication errors related to preventable hospital admissions.[10,11] These agents may increase the risk for harm when used inappropriately in patients hospitalized for acute cardiovascular disorders. One of the 2009 National Patient Safety Goals identified by The Joint

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Table 1. Selected Similar Medication Names in Acute Cardiovascular Practice

Medication	Confused Medication Name
Accupril (ACE inhibitor)	*Aciphex* (proton pump inhibitor)
Activase (fibrinolytic)	*TNKase* (fibrinolytic)
Aggrastat (GP IIb/IIIa inhibitor)	*Argatroban* (thrombin inhibitor)
Calcium chloride	Calcium gluconate
Captopril (ACE inhibitor)	Carvedilol (β-adrenergic blocker)
Cardene (calcium channel blocker)	*Cardizem* (calcium channel blocker)
	Cardura (α-adrenergic blocker)
Dobutamine (sympathomimetic)	Dopamine (sympathomimetic)
Epinephrine (inotrope)	Ephedrine (inotrope)
Isosorbide mononitrate (nitrate)	Isosorbide dinitrate (nitrate)
Lanoxin (digoxin)	Levothyroxine (thyroid)
Metoprolol tartrate (β-adrenergic blocker)	Metoprolol succinate (β-adrenergic blocker)
Nicardipine (calcium channel blocker)	Nifedipine (calcium channel blocker)
Norepinephrine (inotrope)	Neo-synephrine (α-adrenergic agonist)
Pindolol (β-adrenergic blocker)	*Plendil* (ACE inhibitor)
Plavix (antiplatelet)	*Paxil* (antidepressant)
Pravachol (HMG-CoA reductase inhibitor)	Propranolol (β-adrenergic blocker)
Protamine (heparin reverser)	Protonix (proton pump inhibitor)
Tiazac (calcium channel blocker)	*Ziac* (β-adrenergic blocker and diuretic)
Toprol-XL (β-adrenergic blocker)	*Topamax* (migraine prophylaxis)
Tricor (hypolipidemic)	*Tracleer* (endothelin antagonist)
Valsartan (AT2 receptor antagonist)	Losartan (AT2 receptor antagonist)
Zebeta (β-adrenergic blocker)	*DiaBeta* (hypoglycemic)

ACE indicates angiotensin-converting enzyme inhibitor; GP, glycoprotein; HMG-CoA, hydroxymethylglutaryl coenzyme A; and AT2, angiotensin II type 2 receptor.

Information adapted in part from the Institute for Safe Medication Practices' "List of Confused Drug Names," available at http://www.ismp.org/Tools/confuseddrugnames.pdf.

Brand names are italicized.

Commission is to improve the safety of medication use by focusing on reducing the likelihood of harm from anticoagulation.

Medication Omission Errors

Omission of life-saving medications is an underrecognized medication error in the management of patients with acute cardiovascular disease. The proportion of reperfusion-eligible patients presenting with ST-segment elevation myocardial infarction (STEMI) who received immediate reperfusion therapy (either fibrinolytic medications or primary percutaneous coronary intervention) remained only 71% in 2006.[12] Failure to prescribe adjunctive therapies, including antiplatelet agents,[13] β-blockers,[14] angiotensin-converting enzyme inhibitors,[15] and cholesterol-lowing agents,[16] for patients with acute coronary syndrome (ACS) is another example of an error of medication omission.

Errors in the ED

Each year, more than 115 million patients seek care in EDs across the United States. This is the equivalent of 219 ED visits each minute, based on a National Hospital Ambulatory Medical Care Summary.[17] MEDMARX received reports of 29 801 medication errors in EDs from 2002 to 2006. MEDMARX studies showed that 53% of medication errors reached ED patients (in the remaining 47% of cases, the errors were recognized or the medication was not given), 13% of these caused potential harm, and 3% of these resulted in definite harm or death. Substantial patient overcrowding in many EDs, high provider turnover, and language barriers provide an environment that can increase the risk of medication errors. Therefore, simple processes such as adhering to the ACC/AHA guidelines tend to be less effective among EDs where resources are underfunded.[18,19] Caring for critically ill and injured patients with limited information regarding the medical history of the patients also creates a high-pressure environment in which errors in both type and dosage of medications may be more frequent. Finally, the transition of care from one emergency physician to another emergency physician at changes of shift (or from emergency physician to inpatient physician at the time of admission) is a particularly vulnerable time in medical communication that may result directly in medication errors.[20] Medication errors to which ED patients are particularly prone include failure to identify known allergies, failure to identify current outpatient medications that could interact with those provided in the ED, inappropriate type or dosing of medications, incorrect route for administration, an incomplete understanding of variability in dosing for patients with renal insufficiency or diabetes mellitus, and excess dosage for a given body weight, particularly in older women.

Patient Subgroups at High Risk for Errors

Older Adults

Older adults are at a higher risk of medication errors and have a greater propensity for experiencing harmful and fatal errors.[21] The most common types of medication errors among the elderly are those of omission (26%) and improper dose (26%). The use of aspirin, fibrinolytic agents, and heparin acutely and of statins at discharge remains suboptimal even among ideal older adults with acute myocardial infarction with indications for these medications and no contraindications to their use.[22,23] Medication errors of omission are also more likely to occur in elderly patients with ACSs considered to be secondary to another diagnosis. These secondary ACS events are independent predictors of the lack of recommended medication therapy.[24] Omission of evidence-based medications that results from reasonable clinical judgment are of little concern compared with those due to misdiagnosis or misclassification of risk and benefit among those eligible for treatment.

In a population study from 15 000 hospital discharges in 1992, those ≥65 years of age had twice the rate of preventable adverse medication events as those 16 to 64 years old

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(5.3% versus 2.8%, $P=0.001$); however, in multivariable analysis adjusted for comorbidity and case mix, age was not independently associated with preventable adverse events.[25] Rather, older adults are at risk for medication errors for other age-associated reasons. There are very few cardiovascular medications for which doses are adjusted by age alone. In fact, most cardiovascular medication errors in older adults are omission errors.[26]

High rates of polypharmacy also increase the likelihood of drug-drug interactions. Older adults are less likely to receive appropriate follow-up laboratory monitoring for 1 or more of their medications, including angiotensin-converting enzyme inhibitors, amiodarone, and statins.[27] There are age-related changes in pharmacokinetics (eg, medication absorption, metabolism, and hepatic or renal elimination) and pharmacodynamics (eg, reduced baroreflexes and receptor responsiveness), both of which necessitate dose adjustments or heighten susceptibility to medication adverse events. Age tends to be a surrogate for worse renal function, which is important for medications that are cleared renally. Rapid dose escalation may take place during the brief period of acute cardiac hospitalization in an older adult who is also supine and eating a hospital diet, which undermines the advice of "start low, go slow." In addition, the one-size-fits-all approach to dosing of adjustable anticoagulants results in excess dosing disproportionately affecting older adults and contributes to excess major bleeding.[28]

Chronic Kidney Disease

The estimation of creatinine clearance is one of the most important factors that should be readily available to any healthcare provider who prescribes medicines, both in the emergency and the in-hospital setting. Medications such as enoxaparin, eptifibatide, tirofiban, bivalirudin, dofetilide, and sotalol are dosed on the basis of estimated creatinine clearance (eCrCl) with the Cockcroft-Gault formula,[29] not based on the estimated glomerular filtration rate calculated by the Modification of Diet in Renal Disease formula.[30] The 2007 unstable angina/non-STEMI practice guidelines recommend adjusting doses of renally cleared cardiovascular medication on the basis of the eCrCl.[31] The clinical studies and labeling that define adjustments for cardiovascular medication have been based on the Cockcroft-Gault formula, which is not identical to the Modification of Diet in Renal Disease equation. According to the CRUSADE (Can Rapid risk stratification of Unstable angina patients Suppress ADverse outcomes with Early implementation of the ACC/AHA guidelines) study, clinically important disagreements between eCrCl and estimated glomerular filtration rate occurred in one fifth of ACS patients; the authors concluded that medication dosing should be based on the Cockcroft-Gault formula.[32] Although use of the Cockcroft-Gault formula is recommended by the present writing group, this topic remains controversial, because the National Kidney Foundation[33] and the National Kidney Disease Education Program[34] have recommended using either eCrCl or estimated glomerular filtration rate for drug dosing.

Ideally, the eCrCl should be calculated automatically for all creatinine measurements so that eCrCl is provided in addition to the estimated glomerular filtration rate and serum creatinine result. An even more sophisticated system would function such that when electronic prescribing takes place in the hospital, the latest eCrCl would be displayed automatically for all patients for whom a medication was prescribed that requires renal adjustment.[35]

Patients with chronic kidney disease are more susceptible to nephrotoxicity from iodine-based angiographic and gadolinium-based magnetic resonance imaging contrast studies. Strategies to prevent contrast-induced nephrotoxicity should be used for patients undergoing x-ray angiography or computed tomography with iodine-based contrast.[36] The FDA has recently issued a public health advisory stating that exposure to gadolinium-based contrast agents increases the risk for nephrogenic systemic fibrosis in patients with acute or stage IV chronic kidney disease (glomerular filtration rate <30 mL/min) or acute renal insufficiency of any severity.[37] It has been suggested that strategies to prevent contrast-induced nephrotoxicity or an alternative imaging method be considered in patients with stage IV or V chronic kidney disease who undergo angiography with an iodine-based contrast agent or magnetic resonance imaging with a gadolinium-based contrast agent.

Weight-Based Medication Dosing

Although patients admitted to the intensive care unit can be weighed accurately with hospital bed scales, this is not practical for a significant proportion of critically ill patients presenting to the ED. Accurate weight assessment is a challenge for ED patients who are incapacitated. Because many acute cardiovascular medications are dosed according to actual (and not ideal) body weight, overestimation and underestimation of body weight constitute an important source of medication errors that result in adverse medication events and ineffectiveness, respectively. Examples of acute cardiovascular medications that require accurate weight assessment include unfractionated heparin, low-molecular-weight heparin, glycoprotein IIb/IIIa receptor antagonists, fibrinolytic agents (eg, alteplase and tenecteplase), inotropes (eg, dobutamine), vasopressors (eg, dopamine and norepinephrine), vasodilators (eg, nesiritide and nitroprusside), and the inodilator milrinone.

Several studies have examined the accuracy of patients, paramedics, nursing staff, and medical staff in estimating weight in patients brought to the ED. In 1 study, although patients had a mean absolute error of only 3 kg in their estimation of body weight, paramedics, nurses, residents, and attending physicians had a mean absolute error of 9 to 10 kg.[38] Although only 1.5% of patient weight estimations were more than 20% off, 13% to 17% of healthcare providers' estimations were inaccurate by more than 20%. Other studies agree that weight estimation by medical staff is a potential contributor to medication errors.[39,40] These errors are more pronounced in patients at extremes of body weight.

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In critically ill obese patients, noninvasive blood pressure assessment is not reliable. In hypotensive and hypertensive obese patients in the acute care setting, noninvasive blood pressure recordings tend to be inaccurate, which leads to erroneous interpretations of blood pressure and potentially could lead to treatment errors with vasopressors or antihypertensive medications. One study used direct radial arterial blood pressure measurement as the gold standard, and noninvasive blood pressure measurement by the auscultatory technique (calibrated aneroid manometer) significantly overestimated the true blood pressure.[41] Automated noninvasive blood pressure measurements with the oscillometric technique significantly underestimate blood pressure in hypertensive patients. Therefore, in critically ill obese patients, invasive blood pressure monitoring should be instituted rapidly in the critical care setting.

Disease-Based Considerations in Risk for Medication Errors

Acute Coronary Syndrome

The most common types of medication errors in this group include medication dose errors (including failure to account for renal dysfunction), omission (failure to either give the medication or to resume treatment), and miscalculation of a patient's weight. In STEMI patients, omission errors are represented dramatically by the relatively low rates of use of immediate reperfusion therapy,[12] aspirin,[42] clopidogrel, angiotensin-converting enzyme inhibitors,[15] β-blockers, and statins during hospitalization.[43] For the acute administration of intravenous β-blockers in STEMI patients, guideline recommendations have changed recently.[44] Because of an increased risk of cardiogenic shock in patients treated with intravenous β-blockers, current recommendations now advise the avoidance of therapy in patients with any signs of heart failure and in those at increased risk of developing heart failure. What previously may have been considered an error of omission may now be considered a medication error if intravenous β-blocker therapy is given to a patient with evidence of heart failure, because of the increased risk of cardiogenic shock.

The non-STEMI population tends to be an older population with greater comorbid illnesses, worse renal function, and a higher proportion of women. These characteristics predispose to untoward medication reactions if appropriate dosing adjustments are not made. In a comprehensive analysis from the CRUSADE National Quality Improvement Initiative evaluating excessive dosing in patients with non–ST-elevation ACS, 42% of patients who were administered an antithrombotic agent received at least 1 initial dose outside the recommended range.[23] The excess dosing was seen with unfractionated heparin (33%), low-molecular-weight heparin (14%), and glycoprotein IIb/IIIa inhibitors (27%). The factors associated with excessive dosing included older age, female sex, renal insufficiency, low body weight, diabetes mellitus, and congestive heart failure. It was estimated that 15% of all major bleeding in this population was attributable to excessive dosing.

The latest quality metrics for patients with acute myocardial infarction include the frequency of excessively dosed heparin, low-molecular-weight heparin, and glycoprotein IIb/IIIa inhibitors; omission of clopidogrel in medically managed patients; the presence of a weight-based heparin-dosing protocol; and the ability to track bleeding events related to anticoagulants.[45] Systems approaches, such as the AHA's evidence-based Get With The Guidelines, have been shown to improve adherence to guidelines, with an emphasis on reducing medication errors of omission and commission.[46] The following section highlights errors in prescribing that are related to specific agents in ACS (Table 2).

Antiplatelet Agents

The dose of aspirin in combination with other antiplatelet and antithrombotic agents is an important topic. The Second International Study of Infarct Survival (ISIS-2) used a 162.5-mg dose, whereas the most commonly prescribed dose in the United States is 325 mg.[47] Observational data suggest that the use of a lower dose of aspirin (81 mg) after discharge for ACS may be safer, particularly when combined with clopidogrel or prasugrel.[48] Although higher doses may be important in the immediate percutaneous coronary intervention setting, the use of lower doses of aspirin might be appropriate when aspirin is used with clopidogrel, because the higher dosing may be associated with more bleeding.[49] Although the recently presented results of the CURRENT-OASIS 7 trial (Clopidogrel optimal loading dose Usage to Reduce Recurrent EveNTs/Optimal Antiplatelet Strategy for InterventionS) found no differences in ischemic or bleeding outcomes at 30 days in an ACS population with low-dose versus high-dose aspirin,[50] that study did not assess the impact of aspirin dose on longer-term bleeding risks with dual-antiplatelet maintenance therapy.

Another area of complexity in aspirin dosing occurs when patients state that they are allergic to aspirin. Although 3% to 4% of patients have been identified as intolerant to aspirin, closer evaluation suggests that only about half are truly allergic to aspirin.[51] Errors of omission that occur when aspirin is withheld in patients who are simply intolerant to aspirin could be avoided with accurate reporting. For those patients with documented allergy to aspirin, desensitization may be an attractive alternative compared with omission.

The frequency of clopidogrel omission in the management of ACS patients has been reported recently. The proportion of non-STEMI patients treated with clopidogrel within 24 hours of admission who did not undergo early percutaneous coronary intervention has increased from 30% in 2002% to 50% in 2005.[52] Adjusted in-hospital mortality was lower in those treated with clopidogrel.

Intravenous glycoprotein IIb/IIIa inhibitors have been a major advancement in ACS management. Even among diverse randomized trials, women and older adults have higher bleeding rates.[53] Up to one fourth of the bleeding risk

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Table 2. Common Medications Errors in Patients With ACS

Medication	Type of Error	Reason for Use	Preventable Adverse Event	Guideline Recommendations[31,44]
Aspirin	Underuse; misuse (errors in dosing)	Primary and secondary infarction prevention	Increased risk of thrombotic and hemorrhagic complications	Discriminate between true aspirin allergy vs intolerance. Consider dose reduction in patients taking clopidogrel.
β-Blocker	Overuse; misuse (errors in dosing, patient selection, timing)	Prevention of reinfarction and arrhythmia	Increased risk of cardiogenic shock, bradyarrhythmias	In STEMI patients, avoid early IV β-blockers in those with hypotension, pulmonary congestion, or PR prolongation and those at increased risk for cardiogenic shock.
Heparin	Misuse (errors in dosing, monitoring, prescribing, transcribing)	Prevention of early reinfarction and infarction progression	Increased risk of hemorrhagic complications	Weight-based dosing algorithms, particularly important when coadministered with fibrinolytics and GP IIb/IIIa inhibitors.
Low-molecular-weight heparin	Misuse (errors in dosing, monitoring, prescribing)	Primary and secondary infarction prevention	Increased risk of thrombotic and hemorrhagic complications	Careful dosing in obese patients and those with renal insufficiency. Ensure proper dosing (IV and subcutaneous) for STEMI patients.
Small-molecule GP IIb/IIIa inhibitor	Misuse (errors in dosing, monitoring, prescribing, transcribing)	Prevention of early reinfarction and infarction progression	Increased risk of thrombotic and hemorrhagic complications	Follow recommended bolus and infusion dose reductions in patients with renal insufficiency for eptifibatide (creatine clearance <50 mL/min) and tirofiban (creatinine clearance <30 mL/min). In obese patients, prescribe on the basis of labeled dosing recommendations for obese patients.
Direct thrombin inhibitor	Misuse (errors in dosing)	Primary and secondary infarction prevention	Increased risk of thrombotic and hemorrhagic complications	For bivalirudin, follow recommended dose reductions in patients with renal insufficiency (creatinine clearance <30 mL/min). Dosing varies for PCI and medical therapy for ACS.
Factor Xa inhibitor	Misuse (errors in dosing)	Primary and secondary infarction prevention	Increased risk of thrombotic and hemorrhagic complications	Fondaparinux is contraindicated if creatinine clearance <30 mL/min.
Fibrinolytic	Underuse (errors of omission); misuse (errors in dosing, patient selection, timing)	Prevention of infarction progression	Failure to achieve reperfusion; increased risk of hemorrhagic complications	Ensure dosing corresponds to proper fibrinolytic (ie, avoid confusing dosing of TNKase and that of tPA).

IV indicates intravenous; PCI, percutaneous coronary intervention; and tPA, tissue plasminogen activator.

difference observed in women is avoidable and attributed to excessive dosing in women.[54] Women receiving glycoprotein IIb/IIIa inhibitors were more likely to receive excessive doses than men (46% versus 17%, $P<0.0001$).

Fibrinolytic Agents

Incorrect dosing of fibrinolytic agents has been reported to occur in 5% to 12% of STEMI patients.[55] The dosing regimens vary significantly for each of the available fibrinolytic drugs, including streptokinase, tissue plasminogen activator (alteplase), reteplase, and tenecteplase. Dosing errors in the Global Use of Strategies To Open occluded arteries (GUSTO)-I trial were 13.5% for streptokinase and 11.5% for alteplase.[56] Importantly, 30-day mortality was higher in those with medication errors for both fibrinolytic agents and placebo dosing. In contrast, dosing errors are significantly lower for the double-bolus agent reteplase and the single-bolus agent tenecteplase.[54,57]

In the ASsessment of the Safety and Efficacy of a New Thrombolytic (ASSENT-2) trial, incorrect dosing occurred in 4.9% of patients receiving alteplase and 3.6% of those receiving tenecteplase.[58] For those treated with tenecteplase, underdosing occurred in 3.1%, whereas overdosing occurred in 1.5%. Compared with those receiving the correct fibrinolytic dose, patients who received underdosing or overdosing were more likely to be older, to be female, to have lower body weight and systolic blood pressure, and to have a higher Killip class, all of which are associated with higher risk. After adjustment for confounding baseline characteristics, alteplase overdosing was no longer associated with higher mortality, in-hospital stroke, or in-hospital major bleeding. Even with accounting for confounding variables, there is a narrow therapeutic window for fibrinolytic agents, with the potential for adverse outcomes in those with dosing errors. Importantly, although fibrinolytic dosing errors need to be minimized, caution should be exerted in concluding that adverse outcomes associated with errors are directly attributable to the dosing errors. Dosing errors for fibrinolytic agents may reflect other systems and performance deficits that may be associated with increased mortality.

Anticoagulant Agents

Anticoagulants account for 4% of preventable adverse medication events and 10% of potential adverse medication events.[59] Nearly half (49%) of fibrinolytic-treated STEMI patients receive an excess dose of unfractionated heparin in

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contemporary practice.[60] Excess dosing is more common in females and those with low body weight.[28] Patients who receive excessive heparin have higher rates of major bleeding and transfusion.[28]

The ACC/AHA guidelines recommend weight-based unfractionated heparin dosing for non-STEMI[31] and STEMI[44] (with fibrinolytic drugs) ACS with an initial intravenous bolus of 60 U/kg (maximum 4000 U) and an infusion of 12 $U \cdot kg^{-1} \cdot h^{-1}$ (maximum 1000 U/h). An important source of dosing error for unfractionated heparin in ACS patients is the higher recommended dosing for patients with acute pulmonary embolism (an initial intravenous bolus of 80 U/kg with a 5000-U maximum, and an infusion of 18 $U \cdot kg^{-1} \cdot h^{-1}$ with a 1300-U/h maximum)[61] and the absence of a bolus dose of unfractionated heparin in stroke patients. In the CRUSADE Quality Improvement Initiative, an excess weight-adjusted unfractionated heparin bolus or infusion was administered 35% of the time.[28] The factors most strongly associated with excess weight-adjusted dosing were older age and female sex. The rate of major bleeding increased proportionally in relation to the dose of unfractionated heparin for both bolus and infusion.[32] These data suggest that closer attention should be paid to dosing by weight rather than using standard bolus therapy and infusion.

Enoxaparin dosing is adjusted on the basis of both weight and eCrCl. Dosing of enoxaparin for patients with STEMI or those undergoing percutaneous coronary intervention includes both intravenous and subcutaneous administration. Variation in enoxaparin administration practices may lead to confusion when ACS patients are treated in the ED or an outside hospital and then transferred to the cardiac catheterization laboratory or another facility for further management. Because there is no widely available point-of-care laboratory test to assess the level of enoxaparin anticoagulation (comparable to the activated clotting time for unfractionated heparin), low-molecular-weight heparin–dosing errors may arise when it is difficult to confirm the dose, route, and timing of administration.

In the CRUSADE Quality Improvement Initiative, 19% of patients treated with enoxaparin received an excess dose, whereas 29% received a lower-than-recommended dose.[62] Patients who did not receive the appropriate dose had worse outcomes, particularly those who received an excessive dose. Again, patients receiving excessive doses were older, smaller, and more likely to be female than patients who received recommended dosing. To date, there has not been sufficient published information regarding dosing errors with other anticoagulants such as fondaparinux and bivalirudin, which are both dose adjusted for renal function. Recently, The Joint Commission National Patient Safety Goal for 2008 aimed at improving the safety of therapeutic anticoagulation in hospitalized patients (Table 3).[63]

Statins

Omission medication errors involving statins are common in patients with ACS.[16] Similar to other classes of agents for ACS management, the initiation of statin therapy in the hospital improves both outcomes and long-term adherence.[64] Simvastatin, atorvastatin, and lovastatin (but not pravastatin or rosuvastatin), for example, are substrates for metabolism by the 3A4, 3A5, and 3A7 P450 cytochromes. Medication interactions may result in increased statin concentrations caused by inhibitors of this cytochrome (ie, diltiazem, verapamil, amiodarone, clarithromycin, and ketoconazole), whereas inducers (ie, phenytoin, pioglitazone, troglitazone, rifampin, and St. John's wort) of this hepatic pathway may reduce statin levels.

Recently, the FDA issued a warning regarding a dose-dependent drug interaction for the coadministration of simvastatin and amiodarone.[65] Although simvastatin has had this warning included in its label since 2002, reports continue to occur related to the increased risk of life-threatening rhabdomyolysis when simvastatin in doses greater than 20 mg daily is coadministered along with amiodarone, leading to elevated simvastatin concentrations. Amiodarone, as well as verapamil and cyclosporine, reduces the clearance of simvastatin up to 4-fold. In patients with acute myocardial infarction, simvastatin is often prescribed in high doses acutely. These patients may have already been prescribed amiodarone before admission, or during admission, for management of supraventricular and/or ventricular tachyarrhythmias.

Acute Heart Failure

Management of the patient with acute decompensated heart failure is one of the most complex medical situations encountered in acute cardiovascular care, yet there is a paucity of literature specifically on medication errors in treating acute heart failure. Despite this, common sense suggests that medication errors are common in these critically ill patients, and the issues and strategies outlined in the present document are applicable to this area of cardiovascular care.

Patients with heart failure are prone to polypharmacy and its associated issues with dosing, timing, and drug-drug interactions. For example, digoxin serum concentrations may be increased by many medications, including antiarrhythmic agents such as amiodarone and dronedarone. In addition, as patients transition from stable heart failure to acute heart failure, institution of vasopressor or inotrope therapy may be necessary. In this setting, care should be taken to decrease or stop dosages of β-blockers or angiotensin-converting enzyme inhibitors in the face of hypotension. Careful monitoring of potassium and magnesium concentrations, as well as renal function, is important for patients receiving diuretics, angiotensin-converting enzyme inhibitors, angiotensin-receptor blockers, and aldosterone inhibitors.[66] Use of standard dosing units in patients receiving intravenous vasodilators, inotropes, and vasopressors may reduce the risk of dosing errors. For example, 2 different norepinephrine infusion dosing recommendations exist: Micrograms per kilogram per minute[67] and micrograms per minute.[68] The existence of 2 different dosing units (one based on body weight and another not based on body weight) for this medication is a source of critical medication dosing errors, resulting in an error (2 orders of magnitude for adults) of dose administration.

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Table 3. Improving Safety of Therapeutic Anticoagulation: Recommendations From The Joint Commission[112] and the Institute for Healthcare Improvement[115]

General recommendations
Use standard concentrations in ED, OR, cardiac catheterization laboratory, and ICU.
Separate like products when using or storing.
Use smallest package, concentration, and dose for floor stock.
Anticoagulation recommendations
Format anticoagulation flow sheets and orders to follow the patient through transitions from hospital to skilled care and to home.
Use a centralized anticoagulant dosing service for inpatients and have a specialized outpatient anticoagulation clinic.
Implement a weight-based heparin protocol.
Use preprinted order forms or ordering protocols for heparin and low-molecular-weight heparin.
Ensure that heparin cannot be administered within 6 to 12 hours of a low-molecular-weight heparin dose.
Dispense the anticoagulant medication from pharmacy only.
Establish guidelines to hold heparin and provide reversal therapy for heparin overanticoagulation.
Minimize available concentrations of heparin and warfarin.
Develop standardized protocols for the initiation and maintenance of warfarin therapy, including vitamin K dosing guidelines for reversal of overanticoagulation.
Develop a bridging protocol, based on evidence, to discontinue and restart warfarin perioperatively/periprocedurally.
Engage patients in oral anticoagulation management by ensuring that they understand how to take warfarin, know other medications that should be avoided, and can identify symptoms that indicate harm.
Develop educational programs and training, at an appropriate literacy level, to include self-monitoring and how to avoid medication and food interactions.
Work with patients to have them carry an accurate list of medications all the time.
Use medication reconciliation to improve handoffs of medication information, such as follow-up INR monitoring when discharging a patient in need of warfarin INR monitoring.
Make information available on laboratory results of coagulation tests such as aPTT, ACT, and INR to determine doses.
Make laboratory results available on the unit within 2 hours, or monitor at the bedside.
Plot INR results vs dose changes on run chart or control chart to improve dosing of warfarin.
Ensure appropriate monitoring and dose management through a centralized inpatient anticoagulation service.

OR indicates operating room; ICU, intensive care unit; INR, international normalized ratio; aPTT, activated partial thromboplastin time; and ACT, activated clotting time.

Patients with acute heart failure, even in the absence of cardiogenic shock, are subject to altered renal and/or hepatic function that may modulate the renal clearance and/or metabolism of medications such as digoxin, lidocaine, milrinone, and statins and anticoagulant and antiplatelet therapies such as low-molecular-weight heparin, glycoprotein IIb/IIIa inhibitors, and warfarin, which may be used in patients with ischemic heart failure. Therefore, careful attention to changes in renal and hepatic function and dose adjustment based on these parameters is essential. With acutely impaired renal function, hyperkalemia may ensue, particularly in the setting of use of aldosterone antagonists, angiotensin-converting enzyme inhibitors, and angiotensin-receptor blockers. It may be necessary to withhold these agents until renal function improves. In contrast, aggressive diuresis should also lead to vigilance for hypokalemia and hypomagnesemia to avoid arrhythmias and adverse medication effects. Lastly, medication errors occur while heart failure patients are being transitioned back to the outpatient setting. Because heart failure medications are titrated rapidly during hospitalization, accurate prescriptions that pay attention to dosing, electrolyte management, and monitoring of renal function are important shortly after discharge.[69] It is well accepted that the institution of optimal heart failure pharmacological therapy during hospitalization is associated with improved outpatient adherence.[70,71]

Acute Stroke

Although published data are limited, the available information suggests that medication errors are common among patients hospitalized for acute ischemic stroke. A retrospective evaluation based on chart review from 234 ischemic and hemorrhagic stroke cases revealed a 19% in-hospital incidence rate of medication errors.[72] Another study of 1440 patients with ischemic stroke that analyzed spontaneously reported errors and adverse events gathered within a voluntary and mandatory event-reporting system found that only 4% of the patients experienced an adverse event due to medication errors during hospitalization.[73] The mean length of hospital stay was 3 times longer in stroke patients with medical adverse events (including medication errors) than among patients who did not develop an adverse event.

Stroke is a severe medical condition that demands involvement of providers from multiple disciplines, including emergency physicians, stroke specialists, radiologists, vascular surgeons, nurses, imaging and laboratory technicians, and pharmacists. Failure of communication and coordination appears to be an important source of medication error.[74,75] In addition, there are various factors that are associated with increased vulnerability to medication errors in stroke populations. These include advanced age, altered level of consciousness, impaired communication because of aphasia, invasive nature of diagnostic evaluations, high prevalence of comorbid conditions, coadministration of multiple medications, use of intravenous route of administration because of impaired oral intake, administration of medications that require frequent laboratory testing and dose adjustments, and long hospital stay. Specific examples of medication errors for which stroke practice guidelines constantly report cautionary notes are presented in Table 4.

Intravenous alteplase is currently the only FDA–approved treatment for use in acute ischemic stroke.[76] Importantly, the dosing regimen of alteplase for STEMI and stroke patients differs. The most feared complication of treatment with alteplase in acute stroke is symptomatic

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Table 4. Common Medications Errors in Patients With Ischemic Stroke

Medication	Type of Error	Reason for Use	Preventable Adverse Event	Guideline Recommendations[74,75]
IV tPA	Underuse; misuse (errors in dosing, patient selection, timing)	Acute stroke treatment	Increased risk of hemorrhagic complications	Administer at the dose of 0.9 mg/kg (maximum 90 mg) within 4.5 hours of onset in patients who qualify for treatment. Rigorous BP control for 24 hours (keep BP <180/105 mm Hg during and after infusion). Avoid anticoagulants and antiplatelet agents within the first 24 hours
Heparin	Overuse; misuse (errors in dosing, monitoring, prescribing, transcribing)	Prevention of early stroke recurrence and stroke progression	Increased risk of hemorrhagic complications	Not recommended, even for those with AF
Warfarin	Underuse; misuse (errors in dosing, monitoring, prescribing)	Primary and secondary stroke prevention in AF	Increased risk of thrombotic and hemorrhagic complications	Commence anticoagulation with adjusted-dose warfarin (target INR 2.0 to 3.0) in patients with ischemic stroke with persistent or paroxysmal AF
Antihypertensive medications	Misuse (excessive BP reduction in the setting of pressure-sensitive stroke)	High BP during the acute period	Possible infarct progression	Lower BP only if >220/120 mm Hg with a goal to reduce by ≈15% during the first 24 hours of stroke, except for organ dysfunction that necessitates rapid reduction and fibrinolytic therapy
Combination antiplatelets (aspirin-clopidogrel combination)	Overuse (unproven indication)	Secondary stroke prevention	Increased risk of hemorrhagic complications	Not recommended unless there is a specific indication (stent procedure or ACS)
Corticosteroids	Misuse (unproven indication)	Brain edema	Increased risk of infection and other steroid-related complications	Not recommended
Mannitol	Misuse (errors in dosing, timing, and patient selection)	Brain edema	Acute renal failure, exacerbation of congestive heart failure, electrolyte imbalance	0.25 to 2 g/kg IV administered over 20 minutes unless there is frank congestive heart failure or renal failure
IV infusion of hypotonic solutions (NaCl 0.45%, glucose 5%)	Misuse (error in dosing)	Hydration, hypoglycemia	Brain edema	Not recommended
Gadolinium-based MR contrast agents	Overuse (error in patient selection)	Contrast MRI	Nephrogenic systemic fibrosis	Carefully weigh the benefits and risks in patients with acute renal failure or chronic kidney disease (GFR <30 $mL \cdot min^{-1} \cdot 1.73\ m^{-2}$) or acute renal insufficiency of any severity due to hepatorenal syndrome or in the perioperative liver transplantation period. For patients receiving hemodialysis, consider prompt hemodialysis after administration of the MRI contrast

BP indicates blood pressure; AF, atrial fibrillation; MR, magnetic resonance; MRI, magnetic resonance imaging; and GFR, glomerular filtration rate.

intracranial hemorrhage, which occurs in approximately 5% of patients treated. Strict adherence to protocol guidelines is recommended to reduce the risk of hemorrhagic complications.[75,76] The 2009 updated science advisory has recommended increasing the use of alteplase from 3 hours to 4.5 hours from symptom onset.[77] Guidelines also require careful assessment of clinical conditions that are associated with increased risk for hemorrhagic complications and demand that brain computed tomography, blood testing, and electrocardiography be performed before alteplase therapy is administered. Similar to fibrinolysis for STEMI patients, it is not necessary to withhold alteplase until baseline laboratory testing for thrombocytopenia or coagulopathy is completed if the clinical suspicion for these disorders is low. Because time is a critical determinant of treatment effectiveness,[78] it is recommended that fibrinolysis be initiated within 60 minutes of hospital admission.[67] This narrow therapeutic window inevitably leads to deviations from protocol guidelines. Early reports of postmarketing experience with intravenous alteplase demonstrate up to a 50% incidence of protocol deviations.[79] More recent studies report lower but still significant rates that range from 14% to 34%.[80,81] Common protocol deviations include start of treatment beyond the approved time window, failure to maintain blood pressure below desired limits during and after treatment, administration of alteplase despite abnormal baseline coagulation tests, and administration of heparin and antiplatelet agents during the first 24 hours after treatment. Less commonly reported medication errors with alteplase include overdose (because

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the alteplase dose differs for stroke compared with STEMI patients),[81,82] absence of baseline computed tomography, misinterpretation of computed tomography findings,[82] and medication name confusion.[83] Strict adherence to protocol guidelines is critical, because deviations are associated with a more than 2-fold increase in the risk of symptomatic intracranial hemorrhage.[82,84,85] Once intracranial hemorrhage occurs, the likelihood of functional independence is trivial, and the probability of survival is only 20% to 50%.[80–82]

Intravenous fibrinolysis with alteplase is substantially underused in ischemic stroke. A recent study of 366 194 ischemic stroke admissions to US hospitals between 1999 and 2004 found a treatment rate of only 1%.[86] Other reports also show that only approximately 1% to 2% of patients with ischemic stroke are being treated with alteplase.[81,87,88] The mean annual number of patients treated with alteplase per hospital in the United States is only 3. This limited experience of emergency physicians and nurses with stroke fibrinolytic therapy protocols appears to be an important contributor to the occurrence of errors. The implementation of systems that provide an integrated response by neurologists, emergency physicians, nurses, and emergency medical services personnel could not only diminish this source of error but also increase the use of fibrinolytic agents[89,90] and improve patient care and outcomes.[91]

Despite guidelines issued by the AHA/American Stroke Association on the early management of ischemic stroke stating that urgent anticoagulation with heparin is not recommended for the treatment of patients with acute ischemic stroke,[76] physicians continue to use heparin in a substantial proportion of patients to prevent infarct progression and stroke recurrence.[92,93] There is currently no evidence that indiscriminate use of heparin offers a net benefit in the management of acute ischemic stroke.[94–98] On the contrary, heparin treatment is associated with a high rate of hemorrhage.[73,74] Most errors with heparin administration occur as a result of its unpredictable pharmacokinetics, the need for frequent laboratory testing and dose changes, and prolonged continuous infusion. A weight-based nomogram developed for the use of heparin in stroke also appears to reduce the need for frequent dose adjustments and hemorrhagic complications.[99]

In contrast to heparin, anticoagulation with warfarin is substantially underused for both primary and secondary prevention of stroke in patients with nonvalvular atrial fibrillation.[75,76] Several studies have shown that only approximately 50% of patients with nonvalvular atrial fibrillation who have no clinically significant contraindication to anticoagulation receive warfarin.[100–102] Because the therapeutic window of warfarin is narrow and its pharmacokinetics are poorly predictable, the therapeutic range is achieved only 60% of time.[103] Both subtherapeutic and supratherapeutic international normalized ratios are associated with a higher frequency of adverse events (thrombosis and hemorrhage).[104] Advanced age, changes in diet, comorbid conditions, and use of multiple medications that interfere with absorption and metabolism of warfarin appear to be associated with deviations from the optimal international normalized ratio target.[105] There are several anecdotal reports showing that temporary withdrawal of warfarin in patients requiring an invasive procedure (eg, dental extraction, skin biopsy) is associated with occurrence of ischemic stroke.[106,107] A statement issued by the American College of Chest Physicians recommends the use of bridging therapy with heparin or low-molecular-weight heparin during temporary withdrawal in selected patients undergoing invasive procedures.[97] Participation in the AHA's Get With The Guidelines–Stroke[108] and the Stroke PROTECT (Preventing Recurrence Of Thromboembolic Events through Coordinated Treatment)[109] quality improvement programs is associated with improved adherence to warfarin therapy for the secondary prevention of stroke in patients with atrial fibrillation.

Methods to Limit Medication Errors

The recent Institute of Medicine report[4] included recommendations to improve patient outcomes by minimizing medication errors. The Agency for Healthcare Research and Quality has published evidence-based recommendations.[110] In addition, the National Quality Forum,[111] The Joint Commission,[112] the Institute for Safe Medication Practices,[113] the National Coordinating Council for Medication Error Reporting and Prevention,[114] the Institute for Healthcare Improvement,[115] and the American Society of Health-System Pharmacists[116] are among the most widely recognized organizations that have published strategies to prevent medication errors.

Important steps are being taken to begin the process of identification and reporting of medical errors in the ED. Identification of the occurrence of medical errors, followed by voluntary provider reporting, is critical.[117–119] Common definitions of medication error and a blame-free culture that encourages the reporting of errors in the ED can potentially improve care through early recognition of inappropriate treatment.[120]

The National Emergency Department Safety Study is being implemented currently in 85 EDs across the United States affiliated with the Emergency Medicine Network (EMNet).[121] The purpose of this safety study is to identify, characterize, and confirm medication errors for conditions such as STEMI. Studies such as this can identify sources for error, and equally importantly, they can begin to develop a culture for disclosing medication errors in the ED. Because the ED is a complex, high-pressure, high-risk, and sometimes chaotic environment with multiple care providers interacting to deliver medications to critically ill and injured patients, a culture of open communication must exist such that medication errors are identified and disclosed as early as possible after occurrence.

There are 4 points in the medication use process at which errors may occur: (1) The medication is ordered (written, electronic, or oral), (2) the medication order is transcribed and verified, (3) the medication is dispensed, and (4) the medication is administered. There are important interventions related to each of these 4 medication-use

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processes. A cardiovascular pharmacy and therapeutics subcommittee of the larger hospital-based safety committee can focus on managing the cardiovascular medication formulary to increase safety, implement unit dosing, create policies and procedures to ensure compliance with ordering processes, limit verbal orders, ban specific abbreviations and symbols, and develop protocols for high-risk medications.

Medication reconciliation is an important component to reduce medication errors. There are numerous patient handoffs from admission to transfer from the ED, transfers across inpatient units, transfers to procedure suites and operating rooms, and at discharge. In particular, medication discrepancies commonly occur at hospital discharge and are associated with an increased risk of adverse medication events.[122,123] Reconciliation is feasible when medication data are transmitted electronically among providers, with patient confirmation. The following 3 steps are required: First, an accurate and complete medication and allergy list must be compiled. Second, the data must be structured into components, including medication name, dose, route, frequency, duration, and start date. Third, these data must be formatted to allow disparate computer systems to understand both their content and structure.

Most organizations recommend implementation of technological interventions, including computerized provider order entry (CPOE) with clinical decision support and bedside bar coding. Other specific interventions with broad support include implementation and utilization of unit dosing, programmable infusion pumps with flow protection, inclusion of clinical pharmacists in patient rounds, standardization of prescription writing and elimination of certain abbreviations, utilization of written protocols for high-risk medications, and standardization and limiting of verbal medication orders. Additional general recommendations include the adoption of a systems-oriented approach to medication errors, the creation of a culture of safety, and improvements in medication error identification and reporting.

In a 2007 survey, 10% of all hospitals and 26% of hospitals with more than 400 beds had CPOE with clinical decision support.[124,125] In an analysis of 10 studies that evaluated CPOE with clinical decision support, rates of medication errors were reduced by 13% to 86%, and rates of preventable adverse medication events were reduced by 17% to 62%.[4] Dosing guidance, medication-allergy checking, and duplicate-therapy checking are standard mechanisms to reduce common prescribing errors.[126] Advanced dosing-decision support, which takes into account the patient's age, renal function, hepatic function, weight, height, and fluid status, offers additional medication safety features.

Although CPOE with clinical decision support has the potential to deliver benefits, it is clear that computer systems can introduce errors and potentially worsen outcomes in some instances.[127,128] There may be unintended consequences if healthcare providers do not carefully plan and implement major clinical transformations such as CPOE.[129] Continuous monitoring for problems during and after implementation, along with rapid system improvements, is critical.

Role of the Healthcare Team

The process of administering a medication to a hospitalized patient requires many steps and is multidisciplinary. The involvement of attending physicians, physicians-in-training, pharmacists, and nurses as key members of the inpatient healthcare team is critical to minimizing medication errors in patients with acute cardiovascular disease. Good communication is critical as patients transition between the ambulance, ED, intensive care unit, telemetry floor, and outpatient environments to ensure that appropriate dose adjustments and monitoring occur. Physicians-in-training frequently transfer care to on-call teams, which creates another opportunity for medication error in these handoffs. Adverse medication events occur most frequently on the day of admission, in the early morning hours, and during nursing shift changes.[130] The timing of errors emphasizes the importance of effective transitions of care.

Nurses are taught the most important step to ensure safety with respect to administering medications is to check the 5 rights: Right medication, right dose, right time, right patient, and right route. Safety reporting involves the collection, analysis, and dissemination of information on errors, which positively influences patient safety. Root cause analysis and failure mode and effects analysis are 2 multidisciplinary strategies that are often used to examine medication errors. Failure mode and effects analysis is a prospective process, whereas the root cause analysis is reactive in that it occurs after the error and harm. Root cause analyses have resulted in nursing practice changes, including labeling of the infusion pump and the intravenous tubing distally and verification of infusion pumps and associated infusions by 2 nurses at change of shift and whenever new infusions are initiated or the medication concentration is changed. Standardized medication concentrations, either premixed or mixed by the pharmacy, have been found to be helpful in decreasing the number of medication errors.

Smart infusion pumps, bar coding, and personal digital assistant technology are rapidly entering the acute care setting and have been found to be associated with a reduction in medication errors.[131,132] The use of software in a World Wide Web–based intranet that allows the nurse to report a medication error has been found to support this type of culture.[133]

Pharmacist involvement in interdisciplinary cardiovascular or intensive care unit patient-care rounds has been found to increase identification and tracking of medication errors[134,135] and reduce the rate of adverse medication events caused by prescribing errors.[136] Hospitals with pharmacist-provided heparin-management services are reported to have lower mortality ($P<0.0001$), shorter length of stay ($P<0.0001$), lower Medicare charges ($P<0.0001$), and lower rates of bleeding complications ($P<0.0009$) than hospitals without such services.[137]

The ratio of clinical pharmacists to patient beds was associated with a lower hospital mortality rate in an analysis

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of data from the American Hospital Association's Annual Survey of Hospitals and National Clinical Pharmacy Services database of more than 2.5 million patients in 885 hospitals.[138] Pharmacists are integral members of the rapid-response team.[139] Pharmacist participation in the hospital cardiopulmonary resuscitation team was associated with a reduction in hospital mortality rate.[140] Pharmacist-led educational in-service training sessions were found to be an effective way to reduce excess dosing of eptifibatide in patients with renal dysfunction (53% versus 31%, $P<0.001$).[141] Pharmacist participation on cardiac care unit and inpatient teams improves the safety of patients at risk for medication errors. Improved prescribing of angiotensin-converting enzyme inhibitors (90% versus 84%, $P=0.02$) and statins (94% versus 89%, $P=0.02$) was observed when pharmacists were alerted to patients with myocardial infarction through computer alerts for positive troponin values. Pharmacists' review of medications ordered in EDs also has been associated with a reduction in medication errors.[142]

Strategies to improve the safety of high-alert medications include development of a standardized approach to prescribing these medications for common indications through protocols, critical pathways, and preprinted order forms or computerized order sets. The variability in available strengths of parenteral agents also should be minimized.

Reporting of Adverse Medication Errors

Detection, reporting, and analysis of medication errors are essential to ensure patient safety. According to the Institute for Safe Medication Practices, self-reporting strategies remain the most common method for identification of medication errors; however, it is likely that only a minority of medication errors are actually reported. In a prospective single-center study, only 92 (13%) of 731 adverse medication events were detected by physician, pharmacist, and nurse voluntary reporting.[143] The remaining 87% of events were detected with a computerized adverse medication event monitoring system. Computerized adverse medication event surveillance systems detect events at much higher rates than voluntary reporting, and the difference may be greater in community than in academic hospital settings.[144] Compared with chart review, computerized adverse medication event monitoring systems have fair sensitivity (45% to 79%) but poor positive predictive value (11% to 21%), which suggests that the accuracy of computer-based systems still needs improvement.[145,146] The ability to improve reporting systems to detect medication errors is complicated by a litigation system that encourages secrecy. In order for improvements to be made, errors must be reported and analyzed; liability reform must be a component of the overall solution to the problem of medication errors to enable process improvement without fear.[147,148]

Conclusions

Despite being in the national spotlight for most of the past decade, medication errors that affect the management of patients with acute cardiovascular disease continue to be a common and costly problem. Table 5 summarizes the major findings and recommendations from the present scientific statement. Both medication errors of omission and commission constitute important errors in patients with acute cardiovascular illness. In the aging population, numerous medications are prescribed; age-related changes in pharmacokinetics, pharmacodynamics, and renal function require dose adjustments and vigilant surveillance for adverse medication events. Because numerous cardiovascular medications are dosed on the basis of renal function, it is critical to calculate the eCrCl with the Cockcroft-Gault formula on admission for every patient and as changes in body weight and serum creatinine occur. To reduce medication error incidence and its impact, it is critical to integrate nurses and pharmacists into the cardiovascular healthcare team in the ED, intensive care unit, catheterization laboratories, operating rooms, and inpatient wards.

With increasing patient age and the frequent prescribing of multiple medications to acutely ill patients, concerted

Table 5. Recommendations for Medication Safety in Acute Cardiovascular Care

Recommendation	Class (Level of Evidence)
1. An accurate weight should be obtained on admission	I (C)
2. Estimated creatinine clearance should be calculated with the Cockcroft-Gault formula on admission and as changes in creatinine occur	I (B)
3. Because of age-related changes in pharmacokinetics, pharmacodynamics, and renal function, medication dosage adjustments and heightened surveillance for adverse medication events are recommended	I (B)
4. Order forms and protocols for anticoagulation should be standardized	I (B)
5. Pharmacists and nurses should be integrated within the cardiovascular care teams in the ED, ICU, and inpatient wards to enhance communication and medication safety	I (B)
6. CPOE, medication bar-coding technology, and smart infusion pumps should be implemented throughout all inpatient wards, including the ED	I (B)
7. Staff should be educated on high-alert medications (particularly anticoagulants), safe medication administration techniques, medication reconciliation procedures, look-alike/sound-alike medications, and automated dispensing device technologies	I (C)
8. An organizational culture of safety that promotes no-fault internal and external medication error reporting and interdisciplinary quality improvement review processes to reduce the frequency and impact of medication errors is recommended	I (C)

ICU indicates intensive care unit.

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efforts for the prevention, reporting, and management of medication errors must be made nationally. Public reporting of hospital compliance with myocardial infarction and heart failure performance measures has heightened public awareness of medication errors. The current methods for generating and examining information about medication errors are inadequate and limit our understanding of accurate incidence rates and costs of these errors, as well as the efficacy of prevention strategies. The adoption of a number of technologies, including CPOE with clinical decision support, bar coding, and smart infusion-pump technology, is required, particularly in cardiovascular patients treated with high-risk medications such as anticoagulants. These systems are costly to develop and maintain and will require the coordinated support of payers, healthcare providers, insurers, and employers to fund the necessary solutions to avoid medication errors and their consequences.

Key changes in oversight, regulation, and payment are needed to promote improved medication error reporting by all stakeholders, develop minimum functionality standards for error-prevention technologies, and enhance education of healthcare professionals early in their training and throughout their careers to ensure safe medication-management practices. No comprehensive national monitoring system exists for patient safety and medication errors. The Agency for Healthcare Research and Quality has been tasked to set explicit, quantitative, and ambitious goals for patient safety with measurable end points by 2010.[149] To reduce the frequency and clinical impact of medication errors, the medical community must work collectively with The Joint Commission, the National Quality Forum, the American Hospital Association, the American Medical Association, the Leapfrog Group, and all major payers, including the Centers for Medicare and Medicaid Services, to engage patients and caregivers in becoming active partners in safe medication practices, improve and standardize error-detection rates, and implement safer methods to prescribe, dispense, and track medications.

Appendix

Electronic Links to Related Online Resources

Electronic Link	Resource
Medication error reporting	
www.ismp.org	Institute for Safe Medication Practices Medication Errors Reporting System (MERP)
www.nccmerp.org	National Coordinating Council for Medication Error Reporting and Prevention
www.usp.org/hqi/patientSafety/medmarx	US Pharmacopeia's MEDMARX, a national, Internet-accessible database that hospitals and healthcare systems use to track and trend adverse medication reactions and medication errors. Telephone 800-23-ERROR (800-233-7767)
www.fda.gov/medwatch	US Food and Drug Administration's Safety Information and Adverse Event Reporting Program. Telephone 800-FDA-1088
Additional online sources for medication error information	
www.ahrq.gov	Agency for Healthcare Research and Quality
www.pharmacist.com	American Pharmacists Association
www.ashp.org	American Society of Health-System Pharmacists
www.cihsp.org	California Institute for Health Systems Performance (medication safety section has model plan for medication error reduction)
www.icsi.org	Institute for Clinical Systems Improvement
www.ihi.org	Institute for Healthcare Improvement
www.jointcommission.org	The Joint Commission
www.medpathways.info	Pathways for Medication Safety (tools for reducing medication errors)

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Disclosures

Writing Group Disclosures

Writing Group Member	Employment	Research Grant	Other Research Support	Speakers' Bureau/ Honoraria	Expert Witness	Ownership Interest	Consultant/Advisory Board	Other
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This table represents the relationships of writing group members that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all members of the writing group are required to complete and submit. A relationship is considered to be "significant" if (1) the person receives $10 000 or more during any 12-month period, or 5% or more of the person's gross income; or (2) the person owns 5% or more of the voting stock or share of the entity, or owns $10 000 or more of the fair market value of the entity. A relationship is considered to be "modest" if it is less than "significant" under the preceding definition.

*Modest.

†Significant.

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Reviewer	Employment	Research Grant	Other Research Support	Speakers' Bureau/Honoraria	Expert Witness	Ownership Interest	Consultant/ Advisory Board	Other
Joseph S. Alpert	University of Arizona	None	None	None	None	None	Sanofi-Aventis*	None
Savitri Fedson	University of Chicago	None	None	None	None	None	None	None
Gregg C. Fonarow	University of California Los Angeles Medical Center	NHLBI†	None	GlaxoSmithKline†; Merck/Schering-Plough†; Medtronic†; Pfizer†; Bristol-Myers Squibb/Sanofi†; Abbott†; AstraZeneca*	None	None	GlaxoSmithKline*; Novartis†; Medtronic†; Merck/ Schering-Plough*; Forrest*	None
Pooja Khatri	University of Cincinnati	NIH K23†	None	None	None	None	None	None
Janet Parkosewich	Yale University	None	None	None	None	None	None	None

This table represents the relationships of reviewers that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all reviewers are required to complete and submit. A relationship is considered to be "significant" if (1) the person receives $10 000 or more during any 12-month period, or 5% or more of the person's gross income; or (2) the person owns 5% or more of the voting stock or share of the entity, or owns $10 000 or more of the fair market value of the entity. A relationship is considered to be "modest" if it is less than "significant" under the preceding definition.

*Modest.

†Significant.

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Medication Errors in Acute Cardiovascular and Stroke Patients: A Scientific Statement From the American Heart Association

Andrew D. Michaels, Sarah A. Spinler, Barbara Leeper, E. Magnus Ohman, Karen P. Alexander, L. Kristin Newby, Hakan Ay, W. Brian Gibler, Council on Cardiopulmonary, Critical Care, Perioperative, and Resuscitation, Council on Cardiovascular Nursing and Stroke Council
on behalf of the American Heart Association Acute Cardiac Care Committee of the Council on Clinical Cardiology, Council on Quality of Care and Outcomes Research

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