Medication Errors in Patients With Severe Chronic Kidney Disease and Acute Coronary Syndrome: The Impact of Computer-Assisted Decision Support

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OBJECTIVE: **To evaluate the impact of computerized physician order entry (CPOE) with decision support on the frequency of antithrombotic medication errors in patients with chronic kidney disease (CKD) admitted with acute coronary syndrome (ACS) and to measure what effect it would have on in-hospital bleeding.**

PATIENTS AND METHODS: **We evaluated 80 patients with CKD who were admitted with ACS between January 1, 2009, and December 31, 2010, using either a standardized order set or CPOE with decision support to assess the frequency of medication errors and in-hospital bleeding.**

RESULTS: **Of the 80 patients, 47 were admitted with standard orders vs 33 with CPOE. In-hospital bleeding occurred in 13 patients: 10 in the standard orders group vs 3 in the CPOE group (*P*=.12). In-hospital bleeding occurred in 5 (63%) of 8 patients receiving a contraindicated antithrombotic medication compared with 8 (11%) of 72 patients receiving appropriate medications (*P*=.002); the corresponding length of stay was 12.0 days compared with 6.8 days (*P*=.10). Contraindicated medications were given to no patients in the CPOE group vs 8 patients (17%) in the standard orders group (*P*=.01).**

CONCLUSION: **Medication errors occur frequently in patients with CKD admitted with ACS and result in a high risk of in-hospital bleeding. Use of CPOE with decision support is feasible in the ACS setting and may lead to improved patient safety.**

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ACS = acute coronary syndrome; CKD = chronic kidney disease; CPOE = computerized physician order entry; CrCl = creatinine clearance; GP = glycoprotein; IOM = Institute of Medicine; TIMI = Thrombolysis in Myocardial Infarction

Medical errors are the eighth leading cause of death in the United States, accounting for between 44,000 and 98,000 deaths each year.[1] Medication errors are the most frequent type of medical errors, with more than 1 million serious medication errors occurring annually in US hospitals, 20% of which are life-threatening.[2-4] Cardiovascular medications prescribed to inpatients account for a large portion of these errors, particularly in patients admitted with acute coronary syndrome (ACS).[5] In a recent scientific statement, the American Heart Association identified older adults and patients with chronic kidney disease (CKD) as high-risk groups for medication errors and joined with the Institute for Healthcare Improvement and the Institute for Safe Medication Practices in acknowledging antithrombotic drugs as high-alert pharmacologic treatments that have the greatest risk of causing injury when misused.[6,7] In particular, enoxaparin, a low-molecular-weight heparin, is an anticoagulant that is renally cleared and is not recommended in patients with severe CKD.[6,8,9] Similarly, eptifibatide, a small-molecule glycoprotein (GP) IIb/IIIa inhibitor, is renally cleared and is contraindicated in patients with severe CKD because of the high risk of bleeding complications.[10] Alternative medications that are not renally cleared are available, including unfractionated heparin and abciximab. These medical errors are particularly relevant given the increasing prevalence of CKD and the heightened risk that patients with CKD exhibit for the development of coronary heart disease.[11,12] In a recent study of 22,778 dialysis patients undergoing percutaneous coronary intervention in the United States during a 4-year period, 22.3% received a contraindicated antithrombotic medication, an error that was associated with an increased risk of in-hospital major bleeding.[13]

Computerized physician order entry (CPOE) enabled with decision support has been shown to reduce medication errors and is well-suited for the complex algorithms governing the management of ACS; however, we were unaware of data examining the impact of this technology in patients admitted with ACS.[2,3] Therefore, we sought to evaluate the impact of CPOE with decision support on the frequency of antithrombotic medication errors in patients with severe CKD admitted with ACS and to measure what effect this tool would have on the frequency of in-hospital bleeding.

PATIENTS AND METHODS

We recorded clinical characteristics, hospital length of stay, 90-day mortality, and in-hospital bleeding in 80 consecutive ACS patients with severe CKD admitted to the Ochsner Foundation Hospital from January 1, 2009, to December 31, 2010, without a palliative care designa-

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TABLE 1. **Baseline Characteristics in Patients With Severe CKD Admitted With ACS**

	CPOE with decision support (n=33)	Standard orders (n=47)	*P* value
Age (y), mean ± SD	67±15	72±13	.16
Male sex, No. (%)	19 (58)	29 (62)	.73
GFR (mL/min/1.73 m²), mean ± SD	12.9±9.0	15.7±6.8	.15
NSTEMI, No. (%)	25 (76)	35 (75)	.56
TIMI risk, mean ± SD	4.2±1.7	3.5±1.4	.05
Bleeding risk, mean ± SD	59±9	58±10	.90

ACS = acute coronary syndrome; CKD = chronic kidney disease; CPOE = computerized physician order entry; GFR = glomerular filtration rate; NSTEMI = non–ST-segment elevation myocardial infarction; TIMI = Thrombolysis in Myocardial Infarction.

tion. These patients constituted 6.4% of all ACS admissions during that period. The admitting physician (the house officer on duty, whose role was limited to day of admission) had the choice of using preprinted paper orders with check boxes that followed the current American Heart Association/American College of Cardiology guideline recommendations (standard orders) or CPOE with decision support software (a component of the Ochsner Cardiovascular Information System) that generated a paper order set.[14,15] The decision support software required key clinical variables to calculate risk profiles (Thrombolysis in Myocardial Infarction [TIMI] risk, bleeding risk) and generated automatic recommendations for specific therapeutics that the ordering physician could choose to follow or ignore (ie, enoxaparin vs unfractionated heparin, choice of any of the GP IIb/IIIa inhibitors). The decision support software also included drug dosing based on clinical risk, weight, calculated creatinine clearance (CrCl), and consensus guidelines.[14-19] Doses of medications were based on weight and CrCl when appropriate. When severe CKD was present, the decision support software limited physicians in their choice of heparins and GP IIb/IIIa inhibitors to unfractionated heparin and abciximab, respectively, with appropriate alert messages to the physician as to why.

TABLE 2. **Differences in Outcomes by Contraindicated Antithrombotic Medication**

Outcome	Contraindicated antithrombotic (n=8)	No contraindicated antithrombotic (n=72)	*P* value
In-hospital bleeding, No. (%)	5 (63)	8 (11)	.002
Length of stay (d), mean ± SD	12.0±14.3	6.8±7.5	.10
90-day mortality, No. (%)	1 (12)	10 (14)	.70

In-hospital bleeding was defined according to the TIMI bleeding classification as having either a major or minor bleed.[20] Stage 4 or worse CKD was defined as having a calculated glomerular filtration rate less than 30 mL/min/1.73 m².[21] Survival status was obtained from the National Death Index, and ACS was determined from review of the medical record for any discharge diagnosis of myocardial infarction or unstable angina and meeting the appropriate clinical criteria.[22] Chart review and access to the National Death Index were completed in all patients. The protocol was approved by the Institutional Review Board at Ochsner Clinic Foundation.

Statistical analysis was performed using SPSS version 16.0 (SPSS Inc, Chicago, IL). Continuous variables are expressed as mean ± standard deviation; categorical variables as number (%). Differences between continuous variables were assessed using the Wilcoxon rank sum test; differences between categorical variables were assessed using the Fisher exact test. In all analyses, 2-sided $P<.05$ was considered significant.

RESULTS

The mean ± SD age of the 80 patients admitted with ACS was 70±14 years; 60% were male. The mean glomerular filtration rate was 14.5±7.9 mL/min/1.73 m², and 14 patients (18%) were undergoing dialysis. Unstable angina was diagnosed in 11 patients (14%), non–ST-segment elevation myocardial infarction in 60 (75%), and ST-segment elevation myocardial infarction in 9 (11%). The mean TIMI risk score was 3.8±1.6 (range, 1-9), and the mean bleeding risk score was 59±9 (range, 33-82). Forty (50%) of the 80 patients underwent an invasive strategy, whereas the other 40 patients (50%) received only medical therapy. Computerized physician order entry with decision support was used in 33 patients (41%) and standard orders were used in 47 patients (59%) by a total of 35 different physicians (18 using CPOE vs 21 using paper; some used both). Contraindicated antithrombotic medications were given to 8 patients (10%); 1 patient received eptifibatide, and 7 patients received enoxaparin. Of the 7 patients receiving enoxaparin, 1 had CrCl less than 10 mL/min. In-hospital bleeding occurred in 13 patients (16%), of whom 11 had a TIMI minor bleed and 1 a TIMI major bleed. The baseline clinical characteristics of the 2 patient groups are described in Table 1. Other than a higher TIMI risk in patients admitted with CPOE and decision support, there was no statistically significant difference in baseline clinical variables compared with the standard orders group. Patients who received a contraindicated antithrombotic medication had a 6-fold increased risk of in-hospital bleeding (mean hospital day of bleed, 2.4±0.7 days) and a near doubling of the hospital length of stay, with

TABLE 3. **Differences In Outcomes by Admission Order Set**

Outcome	CPOE with decision support (n=33)	Standard orders (n=47)	*P* value
Contraindicated antithrombotic medication, No. (%)	0 (0)	8 (17)	.01
90-day mortality, No. (%)	4 (12)	7 (15)	.50
In-hospital bleeding, No. (%)	3 (9)	10 (21)	.12
Length of stay (d), mean ± SD	4.8±4.0	9.1±10.2	.01

CPOE = computerized physician order entry.

no difference in 90-day mortality (Table 2). Use of CPOE with decision support reduced the frequency of receiving a contraindicated antithrombotic medication and diminished hospital length of stay without altering 90-day mortality (Table 3).

DISCUSSION

The current investigation has 2 key findings. First, prescribing contraindicated antithrombotic medications is not infrequent in patients with severe CKD admitted with ACS, occurring in 10% of our cohort, and is associated with a 6-fold increased risk of in-hospital bleeding. Second, CPOE with decision support is an effective tool in reducing the frequency of medication errors in this population.

Since 2000, when the Institute of Medicine (IOM) issued its report "To Err Is Human: Building a Safer Health System," there has been a greater focus on medical errors, particularly medication errors in hospitalized patients.[1] That same year, 47% of respondents in a US survey of health care consumers indicated that they were "very concerned" about a medical error resulting in injury when they went to a hospital for care, leading Congress to pass the Medicare Modernization Act, which charged the IOM to formulate a national agenda focused on reducing medication errors.[6,23] Although the IOM's report stated that "the problem is not bad people; the problem is that the system needs to be made safer," medication errors continue to occur with significant frequency in patients hospitalized with cardiovascular conditions. A 5-year study reported a rate of 24 medication errors per 100 admissions, attributed primarily to prescribers.[24]

The elderly and patients with CKD have recently been identified as high-risk groups for medication errors in ACS. Similarly, antithrombotics have been identified as medications at risk for causing harm, or "high-alert medications," in ACS.[4,6,7] A recent American Heart Association guideline statement entitled "Medication Errors in Acute Cardiovascular and Stroke Patients" focuses on these facts and further recommends use of CPOE as a system improvement to promote medication safety.[6] To our knowledge, this investigation is the first to assess the impact of CPOE with decision support in a high-risk group in the acute cardiovascular setting.

Key components to this successful implementation were to integrate CPOE with decision support into the daily work flow, provide limited computer support to key decisions, offer recommendations in addition to assessments, and use alert-based or automatic decision support rather than an on-demand system.[25] Limitations to this study were the relatively small sample size and the lack of prospective randomization. Although the use of CPOE with decision support was not randomized, raising the possibility of some selection bias, the baseline characteristics of patients managed with and without CPOE were similar except for a higher TIMI risk in the CPOE group. Therefore, it is possible that the ordering physician was more careful with higher-risk patients, which could have influenced the outcome. Importantly, however, the clinician initiating the orders was generally not the cardiologist managing the patient during hospitalization, thus reducing the chance that this initial choice of orders influenced other aspects of medical care. However, patients did continue the treatment regimen initiated by the admission orders in essentially all cases. As a result, we think that our conclusions remain valid and support the use of CPOE with decision support to promote medication safety in patients with ACS.

CONCLUSION

Our findings support the concept that improving the process of care can lead to meaningful improvements in patient outcomes. We have demonstrated the utility of CPOE with decision support in the ACS process of care, and we suggest that this technology has the potential for improving outcomes in patients with ACS. Further studies are needed to evaluate this technology in larger populations of patients.

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