

Variability of Antithrombotic Dosing Among Veterans Presenting With Acute Coronary Syndrome

Mary E. Plomondon, PhD, MSPH; Anne C. Lambert-Kerzner, PhD, MSPH; Xuefei Jennewein, MS; Katherine Fagan, MPH; Marina McCreight, MPH; Kely B. Fehling, MPH; Thomas T. Tsai, MD, MSc; P. Michael Ho, MD

Background—Antithrombotic therapy for acute coronary syndrome (ACS) patients is recommended by clinical practice guidelines. Appropriate dosing of antithrombotic therapy is necessary to ensure effectiveness and safety and is an American College of Cardiology/American Heart Association ST elevated myocardial infarction/non-ST elevated myocardial infarction performance measure. This study describes the variability in dosing of unfractionated heparin (UH) and low-molecular-weight heparin (LMWH) in an integrated health care system with electronic medical records and computerized physician order entry (CPOE).

Methods and Results—This was a mixed-methods study of veterans presenting with ACS at 135 Veterans Health Administration hospitals from 2009 to 2011. Patients hospitalized with ACS and received antithrombotic therapy were included (n=36 682). The cohort was 98% male with an average age of 66 years and median body mass index (BMI) of 28.6. The average percentage of patients by hospital who received an above-recommended dose of either antithrombotic was 7.5% and ranged 0% to 32.0%. By individual therapy, the average percentage of patients by hospital who received an above-recommended dose of UH was 1.2% and LMWH was 12.9%. Risk-adjusted analyses demonstrated that older age and higher BMI were associated with lower risk for receiving a dose above recommended levels. Additionally, there was an association between antithrombotic ordered by a resident and higher risk of the patient receiving an above-recommended dose. Qualitative interviews supported the quantitative findings by highlighting the need to use current patient weight and the need to adequately train providers on the use of CPOE to improve antithrombotic dosing.

Conclusion—This study found wide hospital variability in dosing of antithrombotics above the recommended level for patients treated for ACS. (*J Am Heart Assoc.* 2015;4:e001433 doi: 10.1161/JAHA.114.001433)

Key Words: acute coronary syndrome • antithrombotic • dosing • quality of care

Acute coronary syndrome (ACS) is a significant cause of cardiovascular (CV) morbidity and mortality in the United States, accounting for over 600 000 hospitalizations a year.¹ Antithrombotic therapy is part of the standard of care for treatment of patients presenting with ACS. As outlined in the American College of Cardiology/American Heart Association (ACC/AHA) ST elevated myocardial infarction/non-ST

elevated myocardial infarction (NSTEMI) clinical practice guidelines and performance measures, there are specific dosing recommendations for anticoagulants in the ACS setting.¹ Previous studies have shown as much as 32.8% of patients receiving excess dosing of antithrombotic therapy among ACS patients.^{2–6}

Potential benefits of an electronic health record (EHR) include improved quality of care, reduced medical errors, increased efficiency through improved accessibility, and reduced cost.⁷ EHRs can reduce medication errors and improve efficiency of the medication ordering process through implementation of computerized physician order entry (CPOE).^{7–9} An earlier systematic review demonstrated decreases in medication errors after implementation of CPOE.⁹ The Veterans Health Administration (VHA) is an integrated health care delivery system with an EHR and CPOE. However, the impact of such tools on antithrombotic dosing among patients presenting with ACS is unknown.

Accordingly, we conducted a mixed-methods study to evaluate the dosing of antithrombotic therapy across VHA hospitals for ACS patients and determine whether specific

From the VA Eastern Colorado Health Care System, Denver, CO (M.E.P., A.C.L.-K., K.F., M.M., K.B.F., T.T.T., P.M.H.); University of Colorado School of Medicine, Denver, CO (M.E.P., A.C.L.-K., T.T.T., P.M.H.); Veterans Health Administration Office of Analytics and Business Intelligence, Inpatient Evaluation Center, Cincinnati, OH (X.J.); Kaiser Permanente Colorado, Denver, CO (T.T.T.).

Correspondence to: Mary E. Plomondon, PhD, MSPH, Cardiology 111B, VA Eastern Colorado Health Care System, 1055 Clermont St, Denver, CO 80220. E-mail: meg.plomondon@va.gov

Received October 24, 2014; accepted April 3, 2015.

© 2015 The Authors. Published on behalf of the American Heart Association, Inc., by Wiley Blackwell. This is an open access article under the terms of the Creative Commons Attribution-NonCommercial License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes.

processes of care at hospitals are associated with dosing antithrombotics consistently with guideline recommendations. Specifically, we assessed the degree of dosing above the recommended dose of unfractionated heparin (UFH) and low-molecular-weight heparin (LMWH) across 135 VHA medical centers for patients presenting with ACS. Second, we assessed the association between patient and provider characteristics with antithrombotic dosing above the guideline-recommended level. Finally, we conducted qualitative interviews at hospitals that had either a high or low proportion of patients who received antithrombotic dosing above guideline recommendations to gain insights into barriers and facilitators to dosing antithrombotic at recommended antithrombotic levels.

Methods

This was a mixed-methods study. To describe the dosing of antithrombotics for patients presenting with ACS, we conducted a national retrospective cohort study of all veterans presenting with ACS at VHA hospitals from 2009 to 2011. We included patients who were hospitalized with ACS, including myocardial infarction (MI) and unstable angina (International Classification of Diseases, Ninth Revision [ICD-9] codes 410 411), from 2009 to 2011 and received antithrombotic therapy (n=53 489). We excluded patients who were missing weight and creatinine measurements (n=4680), missing provider type (n=1149), those who had contraindications to anticoagulant therapy (n=21), and those with missing dose information (n=10 006). Finally, we excluded patients who were given glycoprotein IIb/IIIa inhibitors because we did not feel we could get a full capture of medication usage. The final analytic cohort consisted of 36 682 patients. The Colorado Multiple Institutional Review Board provided a waiver of consent and approval for this study.

Dosing above guideline-recommended level was defined based on the ACC/AHA test performance measures: unfractionated heparin >70 U/kg or infusion >15 U/kg per hour and LMWH >1.05 mg/kg.^{1,2} Data on dose of antithrombotic administered were obtained from the the VHA's barcode medication administration database available through the VHA Inpatient Evaluation Center.

We identified potential factors associated with excess dosing based on literature review and clinical relevance. Patient-level variables included age (≤ 65), gender, race (white/nonwhite), body mass index (BMI), hypertension (HTN), dyslipidemia, previous MI, previous heart failure (congestive heart failure; CHF), previous percutaneous intervention (PCI), previous coronary artery bypass graft (CABG), renal disease, CV disease (CVD), peripheral vascular disease (PVD), chronic obstructive pulmonary disease, diabetes, serum creatinine, type of ACS presentation (MI/unstable

angina), presence of cardiogenic shock, and patient location in the hospital when antithrombotic was first administered (emergency department [ED] vs. floor vs. intensive care unit [ICU]). Provider-level variables included type of provider (hospitalist/internal medicine, emergency medicine, nurse/physician assistant (PA), cardiologist/other specialist, and resident), and hospital-level variables included site, academic affiliation, and hospital complexity designation.

Continuous variables are reported as medians or means and interquartile ranges (IQRs) or SDs. Categorical variables are reported as percentages. Significance testing included chi-squared tests for categorical variables and Wilcoxon's rank-sum tests or *t* tests for continuous variables. The patient-, provider-, and hospital-level factors associated with above guideline-recommended dosing were evaluated using hierarchical logistic regression. Because the primary aim was to identify factors associated with dosing above the recommended level, a dichotomous outcome (above recommended dose vs. not above recommended dosing) was used. Patient and provider factors were entered in the model as fixed effects and hospital factors were entered as random effects to understand the relative contribution of patient, provider, and hospital characteristics associated with dosing of antithrombotics above the recommended level. SAS software (version 9.3; SAS Institute Inc., Cary, CA) was used for all analyses.

For the qualitative analysis, we utilized purposive sampling and conducted individual telephone interviews with inpatient pharmacists and physicians who described the barriers and facilitators to appropriate antithrombotic dosing at select VHA hospitals. Sites were chosen based on the quantitative data, which identified sites that consistently dosed antithrombotics according to guideline recommendations and those that did not consistently dose per guideline recommendations. The interview guide used in this inquiry consisted of 14 semi-structured, open-ended questions to explore the antithrombotic processes at each site. The 30- to 45-minute interviews, conducted by study staff, were audiotaped and transcribed verbatim.

An iterative, inductive, and deductive toolkit of analytical strategies, drawing primarily on content analysis methodology, was used for analysis. To ensure analytical rigor, our qualitative analysts began with repeated readings to achieve immersion followed by initial open coding using an emergent, rather than an a priori, approach. Subsequent analyses utilized a deductive approach based on the literature. The first 2 interviews were independently coded by each member of the analytic team (A.C.L.-K., M.S.M., K.M.F., and K.B.F.). The codes were combined and the analytic team reviewed the documents to clarify meanings of codes and came to consensus when disagreements occurred, thus defining the initial codebook. Emergent codes were added to the codebook throughout this analysis.¹⁰⁻¹³ As patterns, relationships,

and themes emerged and were analyzed, they were reviewed by members of the multidisciplinary research team in order to assess the thoroughness and comprehensiveness of the findings. The computer software program, Atlas.ti (version 6; Atlas.ti Scientific Software Development GmbH, Berlin, Germany), was utilized to organize the coding. In addition, an audit trail was created that documented all analytic procedures and decisions. Finally, we triangulated the results from the qualitative findings, observations we encountered talking with the providers, and quantitative findings.^{11–13}

Results

This was a national cohort study of 36 682 patients admitted with ACS at 135 VHA hospitals between fiscal year (FY)09 and FY11 and administered antithrombotic therapy during their hospital stay. Average number of providers per hospital was 171 with an average of 3 patients per provider. The patient cohort was 98% male with a median (IQR) age of 66 years (IQR, 60 to 77) and a median (IQR) BMI of 28.5 (24.8 to 32.9). Sixty-one percent of the patients presented with acute MI and 39% presented with unstable angina. Most patients had a history of HTN (87%) and hyperlipidemia (73%) and half had a history of diabetes (50%). Unfractionated heparin was given to 62.0% (22 756) patients and 38.0% (13 926) received LMWH. One third of the patients were located in the ICU when the antithrombotic medication was first given (Table).

Among hospitals where a minimum of 25 patients were given an antithrombotic, the mean (SD) percentage of patients receiving a dose above recommended level of either antithrombotic was 7.5% (7.9%) and ranged from 0% to 32%. By therapy across hospitals, the percentage (mean/SD) of patients who received an above recommended dose of unfractionated heparin dose averaged 1.2% (2.2%), ranging from 0% to 9% and among patients who received LMWH averaged 12.9% (6%), ranging from 0% to 32% across hospitals. Figure 1 displays the percentage of patients dosed above the recommended level by hospital for each medication.

In multivariable analyses, the factors associated with dosing above recommended levels varied by specific antithrombotic. In general, these factors included age, BMI, creatinine, location of dose administration, and person prescribing the medication. Older patients (odds ratio [OR], 0.56; 95% confidence interval [CI], 0.41 to 0.77) and patients with higher BMI (OR, 0.96; 95% CI, 0.94 to 0.98) were associated with a lower risk of receiving an initial dose above what is recommended. Additionally, patients with higher creatinine were associated with a lower odds of receiving an unfractionated heparin (OR, 0.88; 95% CI, 0.77 to 0.99) or LMWH (OR, 0.90; 95% CI, 0.83 to 0.98) dose beyond what is recommended. Among the provider and hospital characteris-

tics, there was an association between patients who were first administered LMWH in the ICU (OR, 1.14; 95% CI, 1.01 to 1.28) and prescribed LMWH by a resident (OR, 1.24; 95% CI, 1.07 to 1.45) (rather than hospitalists/internal medicine physician) and higher odds of receiving an initial dose of any antithrombotic that is higher than the recommended dose (Figure 2).

Given the wide range of dosing above recommended levels across hospitals (0% to 32%), qualitative interviews focused on a sample of sites where recommended dosing was most consistently performed and a sample of sites where recommended dosing was least consistently performed. Among the 6 sites contacted, 2 were considered high-performing sites (<10% of patients receiving an antithrombotic dose over what is recommended) and 4 were low-performing sites (≥15% of patients receiving an antithrombotic dose over what is recommended). We interviewed 5 pharmacists (assisted physicians/fellows with dosing of antithrombotics), 1 cardiology fellow (ordered medication and dose), and 1 cardiologist (attending who ordered medication and dose). All but 1 site described some form of antithrombotic dosing guideline for the type and dosing of antithrombotics. Three sites used algorithms in their antithrombotic ordering process that were developed locally and 2 sites followed professional society guidelines (eg, AHA). Five of the 6 sites used specific order sets in the electronic medical records to order and guide antithrombotic dosing. The order sets facilitated prescribing by eliminating the need for physicians to call pharmacists for guidance.

Although most sites indicated that weight was a factor in their dose calculation, the key factor that differentiated high-performing sites from low-performing sites was emphasis on obtaining current patient weights to calculate dose to prescribe antithrombotic therapy. The 2 high-performing sites mentioned their algorithms were developed using the VHA's national safety goal for antithrombotic therapy management. This algorithm emphasized the use of current patient weight and allowed for an independent review of the calculation by a pharmacist. Furthermore, one high-performing site spoke of double checking the patient's weight, whereas some of the least-consistent-performing sites reported using patient self-reported weight or weight recorded in the medical record from the patient's previous visit.

All sites recognized the physician as the decision maker for the antithrombotic dosing process. Although algorithms for dosing are available, only the physician can order medication and dose; therefore, the process must rely on physician availability. The site without a dosing algorithm commented that residents brought tools from the affiliated university (eg, notes and handbooks) to help them choose the type and dose of antithrombotic, a further source of variability. Among sites with order sets, there remained issues such as residents who

Table. Patient, Provider and Hospital Characteristics

Population	No. of Patients		
	Overall (N=36 682)	Unfractionated Heparin (n=22 756)	Low-Molecular-Weight Heparin (n=13 926)
N (No. of hospitals that had at least 1 episode of overdose)	120	36	119
Patient level variables			
Age*	66 (60 to 77)	66 (61 to 77)	65 (60 to 77)
Men	97.96 (35 933)	98.13 (22 330)	97.68 (13 603)
Nonwhite race	23.82 (8738)	25.72 (5852)	20.72 (2886)
BMI*	28.5 (24.8 to 32.9)	28.6 (24.7 to 33.0)	28.5 (24.8 to 32.9)
Hypertension	86.85 (31 857)	87.59 (19 933)	85.62 (11 924)
Hyperlipidemia	73.37 (26 913)	73.20 (16 657)	73.65 (10 256)
Previous MI	28.25 (10 362)	29.08 (6617)	26.89 (3745)
Previous CHF	39.10 (14 341)	41.26 (9390)	35.55 (4951)
Prior PCI	14.69 (5387)	14.39 (3275)	15.17 (2112)
Prior CABG	21.05 (7722)	21.27 (4840)	20.70 (2882)
Renal failure	27.27 (10 004)	32.03 (7289)	19.50 (2715)
CVD	7.73 (2836)	8.06 (1833)	7.20 (1003)
PVD	20.07 (7363)	21.68 (4934)	17.44 (2429)
Chronic pulmonary disease	30.61 (11 230)	30.24 (6881)	31.23 (4349)
Diabetes	50.10 (18 379)	51.46 (11 711)	47.34 (6592)
Serum creatinine*	1.14 (0.90 to 1.60)	1.07 (0.9 0- 1.30)	1.10 (0.90 to 1.40)
ACS type			
ICD-9 411	39.30 (14 415)	36.10 (8214)	44.53 (6201)
ICD-9 410	60.70 (22 267)	63.90 (14 542)	55.47 (7725)
Patient located in ICU when anticoagulant first administered	33.73 (12 374)	35.80 (8146)	30.36 (4228)
Hospital-level variables			
Academic affiliated facility	97.78 (35 869)	99.29 (22 594)	95.33 (13 275)
Hospital complexity			
1a	47.53 (17 435)	53.09 (12 082)	38.44 (5353)
1b	16.44 (6031)	18.93 (4307)	12.38 (1724)
1c	20.61 (7561)	20.20 (4597)	21.28 (2964)
2	12.42 (4555)	7.17 (1631)	21.00 (2924)
3	2.62 (960)	0.57 (129)	5.97 (831)
Excl	0.38 (140)	0.04 (10)	0.93 (130)
Provider-level variables			
Provider type			
Hospitalist and internal medicine	18.55 (6803)	12.87 (2929)	27.82 (3874)
Emergency medicine	1.79 (657)	0.82 (187)	3.37 (470)
Nurse and physician assistant	2.91 (1068)	2.34 (533)	3.84 (535)
Other specialist	2.66 (974)	1.73 (394)	4.16 (580)
Resident (allopathic+osteopathic)	74.10 (27 180)	82.23 (18 713)	60.80 (8467)

ACS indicates acute coronary syndrome; BMI, body mass index; CABG, coronary artery bypass graft; CHF, congestive heart failure; CVD, cardiovascular disease; ICD-9, International Classification of Diseases, Ninth Revision; ICU, intensive care unit; MI, myocardial infarction; PCI, percutaneous intervention; PVD, peripheral vascular disease.

*Presented as median (interquartile range).

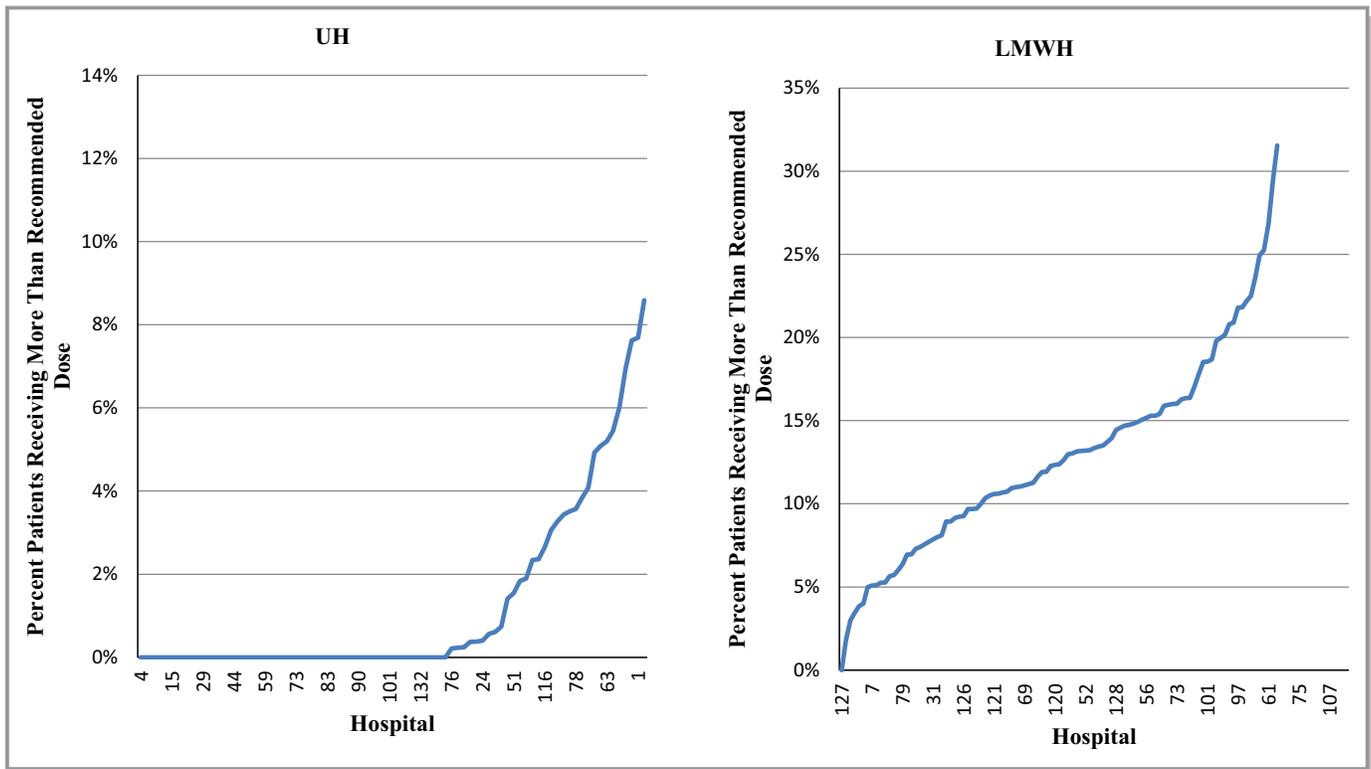


Figure 1. Percent patients dosed above recommended levels. LMWH indicates low-molecular-weight heparin; UH, unfractionated heparin.

were unable to locate the order set within the EHR. One of the high-performing sites acknowledged that, to make the process successful, they needed appropriate dissemination of information:

“... most of our staff that would be ordering this, the vast majority are internists and residents and so making sure that the information is clear, succinct, easy for the provider to order Ideally, we would love for the pharmacists to

order it and to monitor it through their scope of practice . . .”

The sites that dosed least consistently indicated that lack of education was a barrier to appropriate dosing particularly for ACS patients, because “the doses are slightly different, the duration and everything are slightly bit different and so I think that we may need more specialized education regarding that use.”

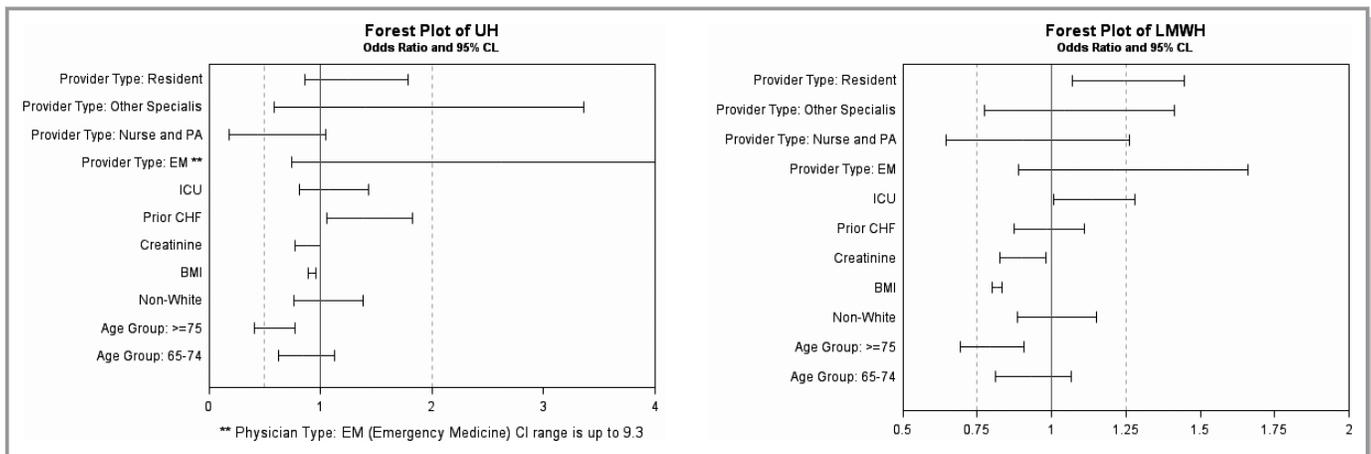


Figure 2. Associations with dosing above recommended levels. BMI indicates body mass index; CHF, congestive heart failure; CI, confidence interval; EM, emergency medicine; ICU, intensive care unit; LMWH, low-molecular-weight heparin; PA, physician assistant; UH, unfractionated heparin.

All 6 sites gave suggestions to improve the antithrombotic prescribing process. Two interviewees thought pharmacists should be able to manage or change medication orders themselves given that they already monitor lab values and thus observe when changes should occur. This would increase efficiency because pharmacists would not have to “hunt down” the physician to make a change. However, to be granted these privileges, a change to their scope of practice would be required as well as better staffing and education. It was suggested that pharmacists be involved during the initial assessment for antithrombotic therapy and a checklist be used to determine appropriate dosing for each patient. Further suggestions included periodic meetings to review the antithrombotic ordering process and make adjustments for improvement.

Through the qualitative evaluation, we found that although most sites had algorithms and order sets available for guidance, not all sites had fully trained residents on their location and use and not all sites verified current patient weights before dosing. In addition, site-initiated, ACS-specific dosing algorithms and order sets were instrumental. The site without algorithms saw there was a need, stating “it [algorithm] was discussed as a future option” and “it [algorithm] is on our perpetual to-do list.” The one site that did not have an order set shared, “I think it would be very helpful. Actually I just hadn’t had the time, but I think it would be extremely helpful.”

Discussion

The aim of this study was to evaluate the variability and processes of care associated with appropriate antithrombotic dosing across VHA hospitals for ACS patients. We found wide hospital variation in dosing above recommended levels of antithrombotics for patients treated for ACS. Furthermore, we found that lower BMI was associated with higher risk of receiving an initial dose of antithrombotic that is above the recommended dose. This finding was corroborated by our qualitative interview findings, which demonstrated sites that verified current patient weights dosed more appropriately. Although weight likely accounts for some of the excess dosing, given the range of excess dose (LMWH, 1.09 to 1.14; UFH, 17.5 to 25.0), it is unlikely to fully explain dosing above the recommended level. We additionally found an association between the type of provider who ordered the therapy (ie, a resident rather than physician, specialist, or nurse) and a higher likelihood of receiving a dose above what is recommended. Again, this finding was corroborated in the qualitative interviews given that interviewees discussed issues with residents who were unable to locate the order sets in the electronic medical record. The wide variability in dosing among hospitals nationally presents an opportunity to

improve dosing through processes such as more diligently checking patient weights and improving availability of dosing guidelines for all providers.

Similar to earlier studies, we found significant variation in antithrombotic dosing. A study using data from the CRUSADE (Can Rapid Risk Stratification of Unstable Angina Patients Suppress Adverse Outcomes with Early Implementation of the ACC/AHA Guidelines) registry found that opportunities to provide guideline-recommended care were missed one quarter of the time.³ An additional study, also using data from the CRUSADE registry, investigated dosing of antiplatelet/antithrombin agents and found that 42% of the patients presenting with NSTEMI were given at least 1 dose beyond the recommended range.² Dosing of unfractionated heparin above recommended levels occurred in 32.8% of the patients and LMWH in 13.8% of patients. Compared to earlier studies, the rates in our study, in a setting with computerized physician order entry, were lower.

The VHA has utilized EHRs since the 1970s and CPOE since 1998. In contrast, less than one third of U.S. hospitals had begun using computerized physician order entry by 2008.^{7,9,14} Although the use of CPOE has been found to reduce medication error by 12.5%,⁹ a poorly designed CPOE has been associated with increased errors owing to poor interface.⁸ All the sites interviewed in our study discussed the value of the EHR and CPOE for antithrombotic dosing. Furthermore, sites that had higher percentages of patients dosed above the recommended level emphasized the need for more thorough training of residents regarding location and use of the EHR antithrombotic guidelines and order sets. Although the rates of dosing above recommended levels in this study were lower, compared to earlier studies, there exists variability of antithrombotic dosing across sites, suggesting the need to understand what processes of care in addition to CPOE can further reduce the variability.

Increased compliance to guideline-based care has been linked to the use of CPOE⁹ and, importantly, increased compliance to guideline-based care has been linked to improved patient outcomes.³ Although guidelines for dosing antithrombotics are available, adoption of the guidelines remains inconsistent.^{15,16} Our study found that administration of antithrombotics by a resident was associated with receiving a higher-than-recommended dose. This finding may reflect lack of training on the location of the CPOE tools in the EHR or may reflect inconsistencies in adoption of the guidelines. EHRs provide an opportunity for guideline dissemination and implementation through tools such as clinical decision support and CPOE. Previous studies have shown that EHRs with CPOE entry tools improve compliance to guidelines^{7,8} and can decrease medication errors.⁹ However, poorly designed CPOE systems with lack of flexibility have been

associated with increased medication errors owing to poor interface and/or lack of training.⁸ Training is likely more challenging for residents who often work in multiple environments with different EHR and CPOE systems. Guidelines have been established for antithrombotic dosing, and, by 2013, more than two thirds of U.S. hospitals had EHR systems that include CPOE, a 5-fold increase since 2008.¹⁴ The challenge remaining, however, is full adoption of guidelines and CPOE by the provider.

There are several limitations to our study. First, dosing information was not available on all patients. However, the missing dosing data were present across all hospitals with no systematic differences and therefore less likely to introduce bias. Second, the data on patients who received IIb/IIIa were incomplete, and therefore we were unable to report on patients who received IIb/IIIa. Third, we were unable to evaluate adjustments to antithrombotic dosing. However, unlike unfractionated heparin dosing, which is followed for adjustment using patient lab values, LMWH dosing is not followed using patient lab values and the dose cannot be adjusted once given. Importantly, previous studies have found that provider adherence to adjustment for infusion maintenance is less than 50%.⁴ We were unable to link dosing above the recommended level to patient outcomes, such as bleeding. Other studies have been published showing association between excess dosing and bleeding.^{2,4,5} Finally, although not a focus of inquiry in this study, underdosing is an important clinical issue that should be addressed in future studies.

Conclusions

Using both quantitative and qualitative methodology, this study found hospital variability in dosing of antithrombotics above the recommended level for patients treated for ACS, which was associated with patient characteristics (younger age and lower BMI), and residents (rather than ED physician, specialist, or nurse) prescribing the therapy. Based on the quantitative and qualitative findings, specific target areas for quality improvement include the following: (1) targeted training for providers (ie, residents) on availability and use of computerized physician order sets within the EHR and (2) using accurate patient information for appropriate dosing, such as direct patient weights obtained at the time of ordering the medication.

Disclosures

None.

References

- Braunwald E, Antman EM, Beasley JW, Califf RM, Cheitlin MD, Hochman JS, Jones RH, Kereiakes D, Kupersmith J, Levin TN, Pepine CJ, Schaeffer JW, Smith EE III, Steward DE, Theroux P, Gibbons RJ, Alpert JS, Faxon DP, Fuster V, Gregoratos G, Hiratzka LF, Jacobs AK, Smith SC Jr. ACC/AHA 2002 guideline update for the management of patients with unstable angina and non-ST-segment elevation myocardial infarction—summary article: a report of the American College of Cardiology/American Heart Association task force on practice guidelines (Committee on the Management of Patients With Unstable Angina). *J Am Coll Cardiol*. 2002;40:1366–1374.
- Alexander KP, Chen AY, Roe MT, Newby LK, Gibson CM, Allen-LaPointe NM, Pollack C, Gibler WB, Ohman EM, Peterson ED; CRUSADE Investigators. Excess dosing of antiplatelet and antithrombin agents in the treatment of non-ST-segment elevation acute coronary syndromes. *JAMA*. 2005;294:3108–3116.
- Peterson ED, Roe MT, Mulgund J, DeLong ER, Lytle BL, Brindis RG, Smith SC Jr, Pollack CV Jr, Newby LK, Harrington RA, Gibler WB, Ohman EM. Association between hospital process performance and outcomes among patients with acute coronary syndromes. *JAMA*. 2006;295:1912–1920.
- Kirtane AJ, Piazza G, Murphy SA, Budiu D, Morrow DA, Cohen DJ, Peterson E, Lakkis N, Herrmann HC, Palabrica TM, Gibson CM; TIMI Study Group. Correlates of bleeding events among moderate- to high-risk patients undergoing percutaneous coronary intervention and treated with epifibitide: observations from the PROTECT-TIMI-30 trial. *J Am Coll Cardiol*. 2006;47:2374–2379.
- Motovska Z, Widimsky P, Petr R, Andrasova A, Bilkova D. The time has come for new, more precise guidelines in the treatment of high-risk acute coronary syndromes with heparin. *Circ J*. 2008;72:1674–1679.
- Lopes RD, Alexander KP. Antiplatelet therapy in older adults with non-ST segment elevation acute coronary syndrome: considering risks and benefits. *Am J Cardiol*. 2009;104(suppl):16C–20C.
- Ash JS, Gorman PN, Lavelle M, Payne TH, Massaro TA, Frantz GL, Lyman JA. A cross-site qualitative study of physician order entry. *J Am Med Inform Assoc*. 2003;10:188–200.
- Menachemi N, Collum T. Benefits and drawbacks of electronic health record systems. *Risk Manag Healthc Policy*. 2011;4:47–55.
- Radley DC, Wasserman MR, Olsho LE, Shoemaker SJ, Spranca MD, Bradshaw B. Reduction in medication errors in hospitals due to adoption of computerized provider order entry systems. *J Am Med Inform Assoc*. 2013;20:470–476.
- Graneheim U, Lundman B. Qualitative content analysis in nursing research: concepts, procedures and measures to achieve trustworthiness. *Nurse Educ Today*. 2004;24:105–112.
- Patton M. *Qualitative Research & Evaluation Methods*. 3rd ed. Thousand Oaks, CA: Sage Publications Ltd; 2002.
- Creswell J. *Qualitative Inquiry and Research Design*. 2nd ed. Thousand Oaks, CA: Sage Publications Ltd; 2007.
- Curry L, Nembhard I, Bradley E. Qualitative and mixed methods provide unique contributions to outcomes research. *Circulation*. 2009;119:1442–1452.
- Dustin C, Gabriel M, Furukawa MF. ONC data brief #16, May 2014. Adoption of electronic health record systems among U.S. non-federal acute care hospitals: 2008–2013.
- Chatterjee P, Joynt KE. Do cardiology quality measures actually improve patient outcomes? *J Am Heart Assoc*. 2014;3:e000404 doi: 10.1161/JAHA.113.000404.
- Budaj A, Brieger D, Steg PG, Goodman SG, Dabbous OH, Fox KA, Avezum A, Cannon CP, Mazurek T, Flather MD, Van De Werf F; GRACE Investigators. Global patterns of use of antithrombotic and antiplatelet therapies in patients with acute coronary syndromes: insights from the Global Registry of Acute Coronary Events (GRACE). *Am Heart J*. 2003;146:999–1006.