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Evaluation of Nurse-Managed Heparin Nomogram Adherence After Implementation of an Electronic Health Record–Embedded Heparin Calculator: An Antithrombotic Stewardship Initiative

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Abstract

Background: Therapeutic intensity unfractionated heparin (UFH) infusions require titration to target a therapeutic activated partial thromboplastin time (aPTT) or UFH anti-Xa. At The Johns Hopkins Hospital (JHH) and Johns Hopkins Bayview Medical Center (JHBMC), a computerized nurse-managed UFH calculator was built into the electronic health record (EHR) to improve adherence to institutional nomograms.

Objective: This study evaluated the impact of implementation of an EHR-embedded UFH calculator on nurse-managed UFH nomogram adherence.

Methods: A retrospective, observational cohort study was conducted at 2 institutions within one health system. Patients admitted to adult services who received nurse-managed UFH for at least 4 consecutive hours were included. Patients admitted between March 2019 and March 2021 constituted the pre-implementation cohort and patients admitted August 2021 through August 2023 were included in the post-implementation cohort. The primary outcomes were nurse-managed UFH nomogram adherence, management of critical aPTT results, and therapeutic aPTT achievement.

Results: A total of 2128 patients were included in the pre-implementation cohort and 2517 in the post-implementation cohort. The mean age was 61 for both the pre- and post-implementation cohorts. The post-implementation cohort experienced an increase in adherence to initial bolus dose recommendations when compared with the pre-implementation cohort (85.9% vs 92%, $P < 0.001$) as well as increased adherence to correct initial infusion doses (80.8% vs 95.9%, $P < 0.001$). Infusion dose adjustment error rates were reduced in the post-implementation cohort (4.9% vs 1.5%, $P < 0.001$). Fewer patients experienced nomogram nonadherence errors in the post-implementation cohort (20.2% vs 5.3%, $P < 0.001$). Critical aPTT nomogram adherence improved after calculator implementation for resumption at the recommended dose (72.4% vs 94.0%, $P < 0.001$). However, the time to therapeutic aPTT achievement was similar between pre-implementation and post-implementation cohorts.

Conclusion and Relevance: A stewardship initiative to implement an EHR-embedded nurse-managed UFH calculator significantly increased adherence to nomogram-recommended initial doses and dose adjustments.

Keywords

anticoagulation, unfractionated heparin, adherence, drug monitoring, medication errors, medication safety, therapeutic monitoring

Introduction

Anticoagulants rank among the most commonly implicated medication classes for adverse drug events.[1-3] The Joint Commission included anticoagulants in the National Patient Safety Goal (NPSG) starting in 2008 with the intent of reducing the likelihood of patient harm associated with the use of anticoagulant therapy.[4-7] More recently, the implementation of anticoagulation stewardship programs has expanded nationally with the goal of

decreasing preventable anticoagulant-related bleeds and thrombosis.[8,9]

Unfractionated heparin (UFH) is the most widely used anticoagulant due to its quick onset, short half-life, and reversibility.[10] Therapeutic intensity UFH dosing is initiated with or without an initial weight-based bolus followed by a maintenance infusion which is adjusted to achieve therapeutic coagulation parameters using either activated partial thromboplastin time (aPTT) or anti-Xa activity.[11] The first UFH nomogram was developed in 1991 to aid clinicians in performing dose adjustments for patients on therapeutic heparin infusions.[12] After the Joint Commission introduced the NPSG on anticoagulation in 2008, use of UFH nomograms to guide therapeutic UFH infusion dose adjustments became standard practice.[4-7] The specific personnel responsible for implementing UFH infusion dose adjustments according to nomogram guidance varies across institutions.

Historically, UFH nomograms were provider-driven, but nurse-driven protocols have become increasingly popular due to data suggesting advantages of this titration method.[13] In 1997, implementation of a nurse-driven UFH nomogram demonstrated reduced time to therapeutic aPTT achievement (16 hours vs 39 hours; $P < 0.05$) with fewer dose adjustments when compared with physician titration.[14] In 2018, Schurr et al highlighted the benefits of implementing a nurse-driven UFH nomogram at Brigham and Women's Hospital, including a significant reduction in the time to therapeutic aPTT achievement compared with physician titration (11.7 hours vs 18.7 hours; $P < 0.005$). The percentage of patients achieving therapeutic aPTT within 24 hours also increased from 74% to 89%. Notably, the implementation of nurse-managed UFH nomograms did not result in an increase in critical aPTT values compared with physician titration.[13] Other institutions have reported similar benefits of nurse-managed UFH nomogram implementation.[15]

Despite the benefits of nurse-driven UFH protocols, the risk of human error remains present when interpreting recommended adjustments within a written nomogram. Most recently, a pilot study demonstrated the use of an UFH calculator decreased the incidence of infusion errors in the emergency department of a community medical center.[16] At The Johns Hopkins Hospital (JHH) and Johns Hopkins Bayview Medical Center (JHBMC), a computerized EHR-based UFH calculator was implemented to help increase adherence to institutional nomograms and reduce medication errors. This study aimed to compare UFH nomogram adherence pre- and post-implementation of an EHR-embedded UFH calculator.

Methods

Study Design

A computerized UFH calculator was implemented into the JHH and JHBMC Epic-based EHR in April 2021. A multidisciplinary workgroup comprised of pharmacists, nurses, physicians, informaticists, and one human factors engineer was formed over 1 year prior to implementation. The workgroup was led by a nurse educator, an anticoagulation stewardship clinical pharmacy specialist, and a clinical pharmacy informaticist. The workgroup focused on identifying areas for improvement with the prior approach (paper nomograms), developing build specifications for the UFH calculator, performing validation of the build, and developing necessary policy updates and educational materials for staff to support implementation. The Epic Foundation UFH calculator was adapted with customization to meet institutional needs. After the workgroup developed build specifications, the build was completed by a single clinical pharmacy informaticist and subsequently validated by 1 pharmacist and 1 fourth-year pharmacy student.

Prior to implementation, extensive education was provided to nurses on best practices for EHR-based calculator use. Electronic learning modules outlining pertinent changes were assigned to all adult inpatient nurses and adult inpatient pharmacists. Nurses also received written education outlining key changes in the form of a fast facts document. In addition, select nurses were identified for each adult unit to attend a training session with the opportunity for hands-on use of the EHR-based UFH calculator and to serve as a just-in-time resource during the implementation period. Pharmacists and prescribers also received written education regarding order set changes that accompanied EHR-based nurse-managed UFH calculator implementation. Nurses access the UFH calculator via UFH order(s) on the medication administration record (MAR), initially selecting from a list of workflow guidance buttons which represent the clinical scenario present at that time (eg, initiating infusion, new aPTT result for infusing UFH). Instructions on next steps are provided based on the selected workflow guidance, such as "use initial dose calculator to start a heparin infusion" which refers users to the section displaying the infusion starting dose, or "use dose

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adjustment calculator and enter new aPTT result" which refers users to the section allowing for aPTT result entry by the nurse to obtain dose adjustment instructions.

A retrospective, observational chart view was conducted to compare pre- and post-implementation cohorts. Patients receiving nurse-managed UFH between March 2019 through March 2021 and August 2021 through August 2023 comprised the pre- and post-implementation cohorts, respectively. The study included patients at least 18 years of age admitted to all adult services (comprised of intensive care and floor level of care for medically ill and surgical patients) at JHH or JHBMC who received nurse-managed heparin infusions for at least 4 consecutive hours. Patients receiving nurse-managed UFH during the 4 months immediately following calculator implementation (April through July 2021) were not included to allow time for staff to adjust to the new nurse-managed UFH workflow. Patients who were switched between UFH nomograms during the evaluation period, presented with an elevated baseline aPTT, transferred from outside hospital, underwent cardiac catheterization before UFH infusion initiation, or prescribed the UFH post-coil stent nomogram (pre-calculator cohort only) were excluded. The primary study outcomes were nurse-managed UFH nomogram adherence, management of critical aPTT results, and therapeutic aPTT achievement pre- and post-calculator implementation.

Data Collection

Ethics approval for this study was obtained from the Institutional Review Board. The details of ordered UFH regimens were collected for each included patient up to 48 hours after UFH initiation. The therapeutic aPTT range at JHH and JHBMC is 50 to 80.9 seconds which corresponds to an UFH anti-Xa of 0.3 to 0.7 IU/mL. Both JHH and JHBMC utilize a Siemens analyzer and Actin FSL brand aPTT reagent which remained constant over the study period. Several lots of reagents were tested at each cycle, and the lot selected matched the previous therapeutic aPTT range to keep the nomograms unchanged. Four nurse-managed UFH nomograms are available at JHH and JHBMC: standard goal protocol (aPTT 50-80.9 seconds), standard goal >155 kg protocol (aPTT 50-80.9 seconds), low goal protocol (aPTT 50-65.9 seconds), and acute coronary syndromes protocol (aPTT 50-65.9 seconds). In the post-calculator implementation period, the 2 standard goal nomograms were combined into one, but all dose adjustments and weight categories remained unchanged with this update. Examples of post-calculator implementation nomograms are available in Appendix A. All nomograms instructed the nurse to draw a baseline aPTT at UFH initiation and recheck aPTT 6 hours after UFH initiation or subsequent dose adjustments. Once 2 consecutive aPTT are within therapeutic range, aPTT measurement frequency is spaced to once daily.

Nomogram adherence was assessed in the portion of the overall population who remained on UFH for 48 consecutive hours after initiation. Patients who underwent cardiac catheterization within 48 hours of heparin initiation were excluded. Available heparin ordering options within each nomogram include (1) infusion only, (2) initial bolus, rebolus, and infusion, (3) initial bolus and infusion (pre-calculator only), and (4) rebolus and infusion, and patients receiving any of these combinations of orders were included in the nomogram adherence assessment. A critical aPTT result was defined as an aPTT $>$ 116 seconds for acute coronary syndromes and low goal nomograms and $>$ 126 seconds for standard goal nomogram. Heparin management at the time of the first critical aPTT result during the encounter was assessed for all patients included in the overall cohort. After the first critical aPTT episode, subsequent critical aPTT episodes were excluded from the critical aPTT analysis.

Study Outcomes

Adherence to nomogram-recommended initial bolus and initial infusion dosing were evaluated in addition to subsequent rebolus administrations and infusion dose adjustments. Nomogram adherence was assessed for each aPTT result available during the 48-hour assessment period for patients in the adherence cohort only.

For critical aPTT results, nurses are instructed to pause the infusion, recheck the aPTT every 2 hours until the result falls below a nomogram-specific aPTT threshold, and subsequently restart the UFH infusion at a nomogram-specified reduced dose. Patients who experienced a critical aPTT result were included in the overall adherence assessment but were also evaluated separately for adherence to each step in the critical aPTT management workflow for the first instance of a critical aPTT value only. In addition, therapeutic aPTT achievement within 6, 12, 24, and 48 hours was evaluated for all patients included in the study. For this assessment, the numerator for each timeframe represents the accumulation of patients who achieved a therapeutic aPTT within the specified timeframe (eg, patients who were therapeutic within 6 hours are also included in the numerator for within 12, 24, and 48 hours). The denominator represents all patients who received a UFH infusion during the study period within each cohort. Furthermore, aPTTs obtained at 6, 12, 24, and 48 hours were categorized according to whether they were subtherapeutic, therapeutic, or supratherapeutic. For this assessment, aPTTs were included for each timepoint if they were collected within 1 hour before or 2 hours after the specified time. The denominator for this assessment represents the total number of aPTTs meeting these criteria at each timepoint.

The frequency of erroneous rebolus administration and UFH infusion dose adjustments titrated using the baseline

Table 1. Baseline Demographics.

Characteristic	Pre-implementation cohort (n = 2128)	Post-implementation cohort (n = 2517)	*P* value
Age—y, median (IQR)	63 (21)	63 (20)	-
Male sex, n (%)	1119 (52.6)	1357 (53.9)	-
Race, n (%)			
Black	1008 (47.4)	1219 (48.4)	-
White	966 (45.4)	1113 (44.2)	-
Asian or Pacific Islander	51 (2.4)	57 (2.3)	-
American Indian or Alaskan	6 (0.3)	6 (0.2)	-
Other	90 (4.2)	106 (4.2)	-
Unknown	7 (0.3)	16 (0.6)	-
Nomogram ordered, n (%)			
Low goal (aPTT 50-65.9)	516 (24.3)	676 (26.9)	0.047
Acute coronary syndromes (aPTT 50-65.9)	294 (13.8)	322 (12.8)	0.315
Standard (aPTT 50-80.9)	1285 (60.4)	1478 (58.7)	0.260
Standard > 155 kg (aPTT 50-80.9)	33 (1.5)	41 (1.6)	0.827
UFH infusion ordered, n (%)			
Infusion only	1163 (54.7)	1588 (63.1)	<0.001
Initial bolus, infusion, and rebolus	876 (41.2)	704 (27.9)	<0.001
Initial bolus and infusion	59 (2.8)	34 (1.4)	0.001
Rebolus and infusion	30 (1.3)	191 (7.6)	<0.001

aPTT results was also assessed. Notably, during the post-implementation evaluation period on July 3, 2023, an alert was implemented which fires to nurses entering an aPTT into the calculator for dose adjustment recommendations within 3 hours of infusion initiation to identify aPTT entries likely representing erroneous use of a baseline aPTT value. Thus, to evaluate the impact of the EHR calculator on erroneous baseline aPTT use for UFH titration, the post-implementation cohort was censored to exclude infusion initiations after July 2, 2023.

Statistical Analysis

STATA Statistical Software, version 18, was used to perform statistical analyses (Stata Corp LP, College Station, TX, USA). Comparative statistics were performed using chi-square test for categorical data and Wilcoxon rank-sum test for continuous data. Statistical significance was defined as a *P*-value <0.05. Shapiro-Wilk test was used to assess whether data was parametric or non-parametric.

Results

A total of 4648 patients were included in the study with 2128 included in the pre-implementation cohort and 2517 patients in the post-implementation cohorts. The median (IQR) age for the pre- and post-implementation cohorts was 63 (21) and 63 (20) years, respectively, and 53% were male. The majority of patients were prescribed the standard UFH nomogram and there were no significant differences observed in the specific nomogram ordered between the pre- and post-implementation cohorts (Table 1). Initial bolus prescribing was significantly more common in the pre-implementation cohort. The median (IQR) duration of the heparin infusion in the pre- and post-implementation cohorts was 37.7 (29.9) and 39.2 (30) hours, respectively ($P = 0.632$). The median time to aPTT result availability after sample collection was 49 minutes (IQR = 29).

The adherence cohort was comprised of 831 patients in the pre-implementation cohort and 957 patients in the post-implementation cohort. A significant increase in adherence to nomogram-recommended initial bolus (85.9% vs 92%, $P < 0.001$) and initial infusion doses (80.8% vs 95.9%, $P < 0.001$) was observed in the post-implementation cohort (Figure 1a). Based on all aPTT results reviewed, overall infusion dose adjustment error rates were significantly lower in the post-implementation cohort, 205/4195 (4.9%) versus 54/3582 (1.5%), $P < 0.001$, and fewer patients experienced one or more infusion dose adjustment error in the post-implementation cohort (20.2% vs 5.3%, $P < 0.001$; Figure 1b). Dose adjustment error categorization is displayed in Figure 1b.

A total of 409 and 487 patients were assessed for critical aPTT management adherence in the pre- and post-implementation cohorts, respectively. No difference was observed in adherence to infusion pausing recommendations between groups (94.2% vs 96.5%, $P = 0.224$). After interruption for a critical aPTT result, the infusion was more frequently resumed at the defined aPTT reinitiation threshold in the pre-implementation cohort (99.0% vs 96.2%, $P = 0.01$). However, adherence to infusion reinitiation at the

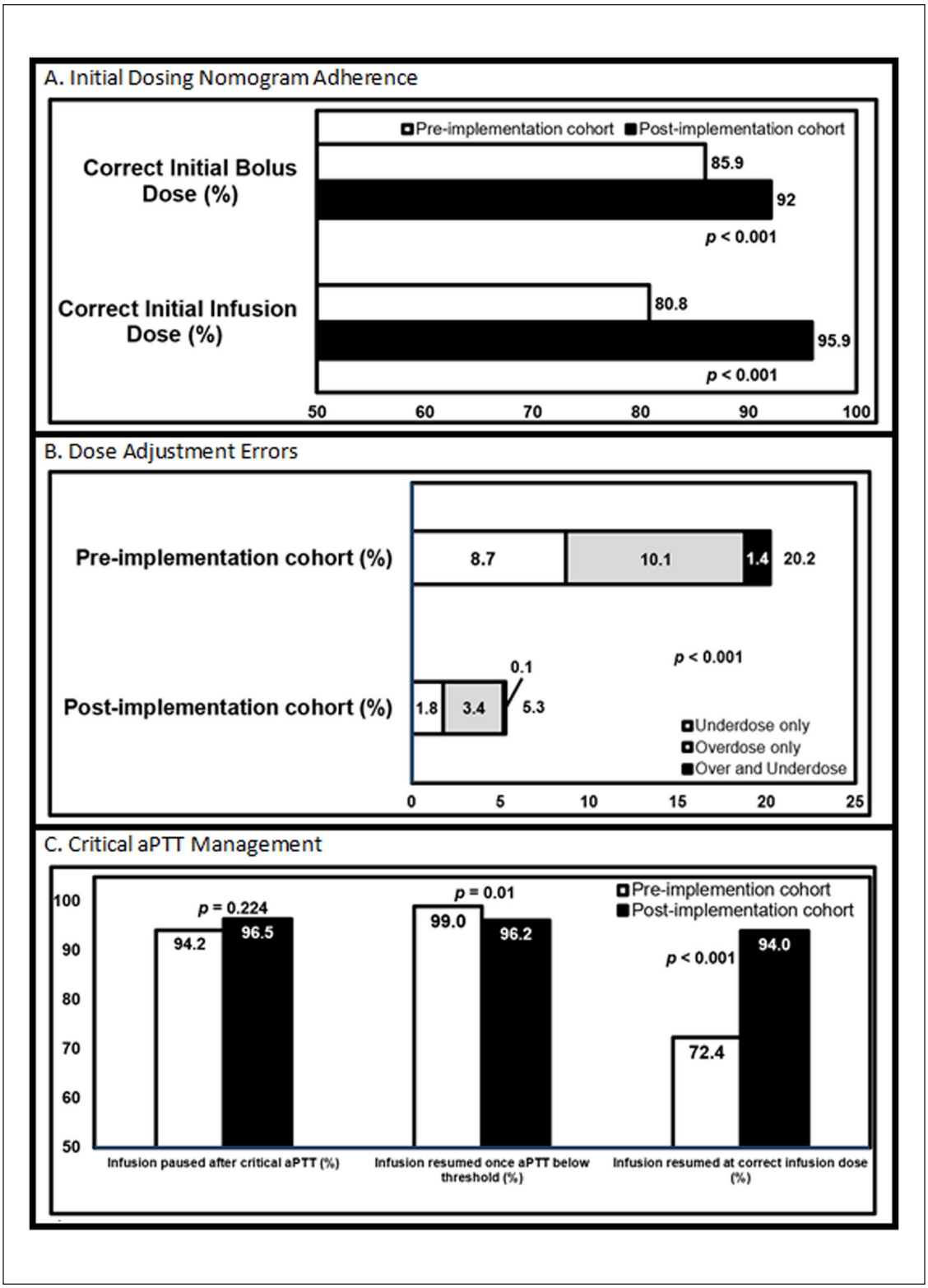

Figure 1. Nomogram adherence. (a) Initial dosing nomogram adherence. (b) Dose adjustment errors. (c) Critical aPTT management.
[a]Initial bolus doses and infusion doses were assessed for correctness based on nomogram recommendations (panel a). Adjustment errors included patients with ≥1 incorrect dose adjustment (panel b). Patients with ≥1 incidence of a critical aPTT result were assessed based on the first critical aPTT episode. Critical aPTT: aPTT > 116 for acute coronary syndrome and low goal; aPTT > 126 for standard goal (panel c).

Table 2. Therapeutic aPTT Achievement.

Endpoints	Pre-implementation cohort (n = 2128)	Post-implementation cohort (n = 2517)	*P* value
Therapeutic aPTT, n (%)			
Within 6 hours	521 (24.5)	601 (23.9)	0.650
Within 12 hours	867 (40.7)	935 (37.2)	0.014
Within 24 hours	1295 (60.8)	1443 (57.3)	0.018
Within 48 hours	1523 (71.6)	1721 (68.4)	0.018
Time to therapeutic aPTT (hours), median (IQR)	13.1 (14.5)	13.3 (15.5)	0.607

Table 3. aPTT Categorization at 6, 12, 24, and 48 Hours Post-UFH Initiation.

aPTT Category	Pre-implementation cohort, n/n total (%)	Post-implementation cohort, n/n total (%)	*P* value
At 6 hours			<0.001
Subtherapeutic	718/1820 (39.5)	900/1972 (45.6)	
Therapeutic	477/1820 (26.2)	508/1972 (25.8)	
Supratherapeutic	625/1820 (34.3)	564/1972 (28.6)	
At 12 hours			<0.001
Subtherapeutic	310/1015 (30.7)	433/1143 (37.9)	
Therapeutic	425/1015 (41.8)	395/1143 (34.5)	
Supratherapeutic	280/1015 (27.5)	315/1143 (27.6)	
At 24 hours			0.398
Subtherapeutic	133/442 (30.0)	176/523 (33.7)	
Therapeutic	208/442 (47.1)	242/523 (46.3)	
Supratherapeutic	101/442 (22.9)	105/523 (20.0)	
At 48 hours			0.020
Subtherapeutic	45/153 (29.4)	68/180 (37.8)	
Therapeutic	89/153 (58.2)	78/180 (43.3)	
Supratherapeutic	19/153 (12.4)	34/180 (18.9)	

nomogram-recommended reduced dose after interruption for a critical aPTT value increased in the post-implementation cohort (72.4% vs 94.0%, $P < 0.001$) (Figure 1c).

Therapeutic aPTT achievement was higher in the pre-implementation cohort within 12, 24, and 48 hours of heparin initiation (Table 2). Notably, the time to first therapeutic aPTT was similar between the pre- and post-calculator cohorts, with a median time of 13.1 and 13.3 hours, respectively. Rates of subtherapeutic, therapeutic, and supratherapeutic aPTTs at 6, 12, 24, and 48 hours after UFH infusion initiation are outlined in Table 3. Notably, significant differences exist between groups at 6 and 12 hours. Numerically higher rates of subtherapeutic aPTTs were observed in the post-implementation cohort at 6 and 12 hours, while the pre-implementation group demonstrated a numerically higher rate of supratherapeutic aPTTs at 6 hours.

A comparison of rates of baseline aPTT utilization for UFH infusion adjustments or rebolus administration was performed between cohorts. For this evaluation, the post-implementation cohort assessment period ended on July 2, 2023, due to implementation of a best practice alert (BPA) directed at this workflow on July 3, 2023 (Table 4). There were no differences between cohorts in the frequency of infusion dose adjustments using the baseline aPTT result. Fewer patients in the pre-implementation cohort erroneously received a single rebolus dose using the baseline aPTT result compared with the post-implementation cohort.

Discussion

Principal Findings

Implementation of an EHR-embedded nurse-managed UFH calculator resulted in a significant increase in adherence to nomogram-recommended initial bolus doses, initial infusion doses, and infusion dose adjustments. This improvement is likely due to removing the need for the nurse to identify the appropriate written nomogram among 4 available protocols and the risk for misinterpretation of the nomogram charts in the pre-implementation cohort. Previously, the nurse was required to manually calculate dose adjustments and navigate between multiple screens

Table 4. Utilization of Baseline aPTT for Infusion Dose Adjustments and Rebolus Administration.

Endpoints	Pre-implementation cohort	Post-implementation cohort	*P* value
Excluding patients in post-calculator cohort after best practice alert implementation[a]			
Infusion dose changed due to baseline aPTT, n/n total (%)	28/2128 (1.3)	27/2427 (1.1)	0.534
Erroneous rebolus given due to baseline aPTT, n/n total (%)	9/516 (1.7)	19/492 (3.9)	0.041

[a]On July 3, 2023, a best practice alert was implemented for an aPTT entered within 3 hours of initiation. The alert recommended the user to verify that the aPTT entered is not a baseline aPTT.

within the EHR (eg, laboratory results, nomogram weblinks, orders tab) to gather all necessary information. With the implementation of the UFH calculator, all the required information is located within the UFH order under the medication administration record. The nurse inputs the appropriate aPTT result into the calculator and is subsequently instructed on whether to administer a bolus, adjust the infusion dose, and when to time the next aPTT lab draw.

Restarting the infusion at an increased dose after the result of a critical aPTT was a common error prior to UFH calculator implementation. Due to misinterpretation of the paper nomograms, the aPTT drawn after infusion interruption which is intended for use in determining when to reinitiate the infusion was mistakenly used to guide dose adjustments. This resulted in inappropriate dose escalation rather than decrease from the original infusion dose which led to the critical aPTT. One advantage of the electronic build of UFH calculator is the ability to implement alerts and/or hard stops to intervene on error-prone workflows. Thus, the UFH calculator was configured to prevent users from entering a new aPTT value into the calculator to obtain dose adjustment recommendations while the infusion is paused for a supratherapeutic result to abate this high-risk error. With this structure, the UFH calculator significantly decreased the percentage of incorrect infusion doses at the time of infusion reinitiation after a critical aPTT by 21.6%. Although there was a statistically significant increase in the frequency of inappropriate UFH reinitiation timing after infusion interruption in the post-implementation cohort, the difference of 2.8% is likely not clinically significant. In addition, the infusion reinitiation timing portion of the critical aPTT workflow was not expected to be impacted by UFH calculator implementation because there are no safety features integrated into the calculator build impacting this specific part of the workflow. Moreover, compliance rates with this part of the workflow were already very high pre-EHR calculator implementation.

Therapeutic aPTT achievement rates within 12, 24, and 48 hours did not favor the post-implementation cohort. Notably, the difference between groups at each of these 3 time points is approximately 3% which may not represent a clinically significant difference, as the overall time to therapeutic aPTT achievement did not differ between groups. When aPTTs obtained at 6, 12, 24, and 48 hours were categorized as subtherapeutic, therapeutic, or supratherapeutic and compared between groups, significant differences were identified between groups at 6 and 12 hours after UFH initiation. Rates of subtherapeutic aPTTs were higher in the post-implementation cohort at 6 and 12 hours, while rates of supratherapeutic aPTTs were higher in the pre-implementation cohort at 6 hours. These differences between groups may have offset and contributed to a similar time to first therapeutic aPTT between groups.

With a decrease in the observed error rate after implementation of the calculator, improved rates of therapeutic aPTT achievement were expected. Further investigation is warranted to determine the driver of this important finding, which seems to be unrelated to calculator performance. More specifically, while nomogram adherence was measured, the timeliness of aPTT obtainment and subsequent dose adjustments were not assessed and represent an important area of additional study. Another potential contributor to these findings is that there were higher rates of prescribing less aggressive dosing strategies in the post-implementation cohort, including use of infusion only orders without an initial bolus or rebolus. It is possible that the numerically higher rates of supratherapeutic aPTTs at 6 hours in the pre-implementation cohort occurred because of increased rates of initial bolus administration in the pre-implementation cohort. In addition, these findings may also be due to performance of our nomograms, because with improved nomogram adherence post-implementation we can more accurately evaluate nomogram adherence and identify opportunities for improvement in our dosing strategies. As such, these results suggest that further investigation is needed to determine whether adjustments to our initial dosing and dose adjustment protocols are required.

Importantly, a higher number of patients in the post-calculator cohort received rebolus dose administration inappropriately based on the baseline aPTT value, rather than the first aPTT drawn after starting the infusion. This issue was identified early after calculator implementation from patient safety event reporting, and a BPA was created in response. The exact reason for the higher frequency of this error after calculator implementation is unknown. We hypothesize that in the pre-implementation cohort, there was a higher rate of rebolus dose omission due to the need to refer to 2 separate pages of the nomogram for the rebolus

and infusion instructions. Therefore, the rebolus omission error prevented the interpretational error of basing rebolus doses on the wrong aPTT. Despite the BPA being added to the calculator workflow on July 3, 2023, the impact of this alert was not assessed due to the small sample size in the post-alert period. Subsequent to the time period evaluated in this study, the aPTT entry field on the rebolus order was removed as an additional safety feature, forcing the nurse to use the EHR calculator on the infusion order to determine both infusion dose adjustments and rebolus recommendations. This helps to ensure that the safety features anchored on the infusion order, such as the baseline aPTT BPA, are not incidentally bypassed.

Notable limitations of this study include the challenges associated with retrospective chart reviews, which require proper EHR documentation for data accuracy. In addition, initial bolus and rebolus prescribing patterns were different between cohorts which introduces an important confounder. More patients in the post-implementation cohort received less aggressive dosing strategies, which could have affected time to therapeutic aPTT, although the impact of this was not fully explored in an adjusted analysis. Furthermore, the time from aPTT result availability to dose adjustment and the number of aPTT lab draws were not assessed, which could have affected the rates of and time to therapeutic aPTT achievement. Lastly, interruptions in heparin infusions during the study period which occur in practice due to factors such loss of intravenous access or the need for minor bedside procedures were not captured.

The strengths of this study include the large sample size and multicenter design which evaluated adherence to all dose adjustment aspects of UFH calculator nomogram workflows in a real-world clinical setting. This comparative study not only highlights how the integration of EHR-embedded tool can increase medication safety, but also how it can lay the groundwork for future research and auditing.

Conclusion and Relevance

This is the first, large-scale, multicenter study to demonstrate the impact of an EHR-embedded nurse-managed UFH calculator. The build, implementation, and maintenance of EHR-based heparin calculators are labor intensive, and these findings provide justification for allocation of resources to support these efforts to improve safety. In addition, moving all aspects of calculator recommendations from paper nomograms to the EHR also allows large-scale auditing to guide education and calculator configuration updates. The use of automated systems in medication management continues to rise. This study emphasizes the importance of new technology integration and the validation of its impact.

In our cohort, the implementation of an EHR-based nurse-managed UFH calculator decreased medication errors. Implementation of the EHR-embedded nurse-managed UFH calculator significantly increased adherence to nomogram-recommended initial bolus and infusion doses, as well as subsequent infusion dose adjustments and rebolus dose administrations. A higher portion of patients received the correct initial bolus dose in the post-calculator cohort. The UFH calculator significantly decreased infusion dose adjustment errors, which was largely driven by overdose errors in the pre-implementation cohort and represents an opportunity to reduce supratherapeutic levels and bleeding events with UFH calculator use. Importantly, a concerningly high rate of incorrect doses were observed in the pre-implementation cohort when restarting the UFH infusion following critical aPTT results. The increased rates of infusion resumption at the correct dose observed in the post-implementation cohort within the critical aPTT workflow may potentially reduce bleeding events. Despite these positive results, fewer patients in the post-calculator cohort achieved a therapeutic aPTT within 12, 24, and 48 hours though time to therapeutic aPTT were similar. Additional evaluation is needed to better understand key drivers of this finding such as timeliness of aPTT obtainment, response to aPTT results, and overall nomogram performance. A larger proportion of patients in the post-implementation cohort had an infusion only order, which may have also affected time to therapeutic range. Further evaluation is warranted to evaluate the impact of differences in ordering practices for initial bolus and re-bolus orders on therapeutic aPTT achievement.

These results support implementation of EHR-based nurse-managed UFH calculators as an antithrombotic stewardship initiative to reduce preventable adverse events associated with anticoagulation therapy and improve adherence to institutional nomograms.[17,18]

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Supplemental Material

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References

1. Shehab N, Lovegrove MC, Geller AI, Rose KO, Weidle NJ, Budnitz DS. US emergency department visits for outpatient adverse drug events, 2013-2014. *JAMA*. 2016;316(20):2115-2125. doi:10.1001/jama.2016.16201

2. Authority PPS. Oral anticoagulants: a review of common errors and risk reduction strategies advisory. Pennsylvania Patient Safety Authority. Accessed June 7, 2024. http://patientsafety.pa.gov:80/ADVISORIES/Pages/201506_54.aspx
3. Graves CM, Haymart B, Kline-Rogers E, et al. Root cause analysis of adverse events in an outpatient anticoagulation management consortium. *Jt Comm J Qual Patient Saf*. 2017;43(6):299-307. doi:10.1016/j.jcjq.2017.03.007
4. Dager WE, Ansell J, Barnes GD, et al. "Reduce the likelihood of patient harm associated with the use of anticoagulant therapy": commentary from the anticoagulation forum on the updated joint commission npsg.03.05.01 elements of performance. *Jt Comm J Qual Patient Saf*. 2020;46(3):173-180. doi:10.1016/j.jcjq.2019.12.004
5. The Joint Commission. National patient safety goals NPSG 03.01.05. Accessed Jun 7, 2024. www.jointcommission.org/assets/1/18/NPSG_Chapter_Jan2013_AHC.pdf
6. Institute for Safe Medication Practices. Improving medication safety with anticoagulant therapy. Accessed June 7, 2024. www.ismp.org/tools/anticoagulantTherapy.asp
7. Nutescu EA, Wittkowsky AK, Burnett A, Merli GJ, Ansell JE, Garcia DA. Delivery of optimized inpatient anticoagulation therapy: consensus statement from the anticoagulation forum. *Ann Pharmacother*. 2013;47(5):714-724. doi:10.1345/aph.1R634
8. National Quality Forum (NQF) *Advancing Anticoagulation Stewardship: A Playbook*. NQF; 2022.
9. Dane KE, Streiff MB, Lindsley J, Montana MP, Shanbhag S. The development and impact of hemostatic stewardship programs. *Hematol Oncol Clin North Am*. 2019;33(5):887-901. doi:10.1016/j.hoc.2019.05.010
10. Qiu M, Huang S, Luo C, et al. Pharmacological and clinical application of heparin progress: an essential drug for modern medicine. *Biomed Pharmacother*. 2021;139:111561. doi:10.1016/j.biopha.2021.111561
11. Jia Z, Tian G, Ren Y, Sun Z, Lu W, Hou X. Pharmacokinetic model of unfractionated heparin during and after cardiopulmonary bypass in cardiac surgery. *J Transl Med*. 2015;13:45. doi:10.1186/s12967-015-0404-5
12. Cruickshank MK, Levine MN, Hirsh J, Roberts R, Siguenza M. A standard heparin nomogram for the management of heparin therapy. *Arch Intern Med*. 1991;151(2):333-337.
13. Schurr JW, Stevens CA, Bane A, et al. Description and evaluation of the implementation of a weight-based, nurse-driven heparin nomogram in a tertiary academic medical center. *Clin Appl Thromb Hemost*. 2018;24(2):248-253. doi:10.1177/1076029617721009
14. Brown G, Dodek P. An evaluation of empiric vs. Nomogram-based dosing of heparin in an intensive care unit. *Crit Care Med*. 1997;25(9):1534-1538. doi:10.1097/00003246-199709000-00021
15. Williams TD, Sullivan K, Lacey C, Adoryan S, Watts B. Nurse-driven intravenous heparin protocol: quality improvement initiative. *AACN Adv Crit Care*. 2010;21(2):152-161. doi:10.1097/NCI.0b013e3181d2f2c6
16. Booth DY, Cherian SM, Lark J, Stratton M, Babu RN. Implementation of a heparin infusion calculator in the electronic health record system as a risk-mitigation strategy in a community teaching hospital emergency department. *J Emerg Nurs*. 2024;50(1):36-43. doi:10.1016/j.jen.2023.10.002
17. May JE, Triller DM, Inglis L, et al. Securing administrative leadership commitment for anticoagulation stewardship programs. *J Am Coll Clin Pharm*. 2024;7(4):384-394. doi:10.1002/jac5.1936
18. Burnett AE, Barnes GD. A call to action for anticoagulation stewardship. *Res Pract Thromb Haemost*. 2022;6(5):e12757. doi:10.1002/rth2.12757