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BRIEF REPORT

Electronic alerts to improve management of heparin-induced thrombocytopenia

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Abstract

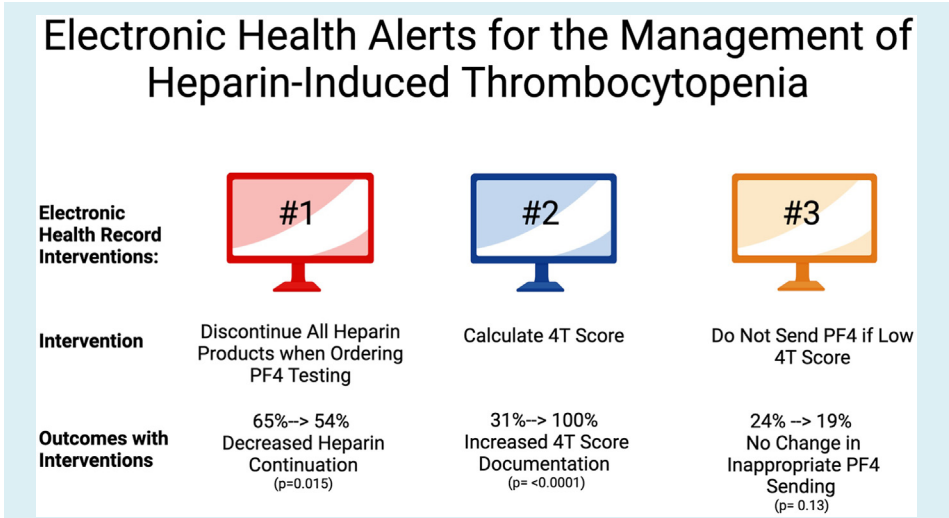
Background: Heparin-induced thrombocytopenia (HIT) is a difficult clinicopathologic diagnosis to make and to treat. Delays in identification and appropriate treatment can lead to increased morbidity and mortality.

Objectives: To use electronic health alert interventions to improve provider diagnosis and management of heparin-induced thrombocytopenia through guideline-based, accurate care delivery.

Methods: This quality improvement initiative developed 3 electronic health record-based interventions at our 750-bed academic medical center to improve the initial management of suspected HIT between 2018 and 2021: 1. an interruptive alert to recommend discontinuation of active heparin products when signing a heparin-platelet factor 4 test (PF4) order, 2. integrated 4T score calculation in the heparin-PF4 test order, and 3. interruptive alert suggesting not to order heparin-PF4 tests when the 4T score is <4. Changes in practice were assessed over defined time periods pre and post each intervention.

Results: Intervention 1 resulted in heparin discontinuation in more patients, with 65% (191 heparin orders/293 heparin-PF4 enzyme-linked immunosorbent assay tests) of cases continuing heparin prealert and only 54% (127 heparin orders/235 heparin-PF4 enzyme-linked immunosorbent assay tests) postinterruptive alert (95% CI 2.3-19.9; P = .015). Intervention 2 increased appropriate heparin-PF4 test ordering from 40.4% (110/272) preintervention to 79.1% (246/311) (95% CI 30.9-46.4; $P < .00001$) post-intervention, with inappropriate PF4 ordering defined as testing when 4T score was <4. Intervention 3 did not lead to reduction in heparin-PF4 testing in the control group (96 inappropriate orders/402 total orders, 24%) compared to the randomized alert group (56 inappropriate orders/298 total orders; 19%) (95% CI −1.2 to 11.5; P = .13).

Conclusion: Implementation of unique electronic health record interventions, including both diagnostic and management interventions, led to improved guideline-based, accurate care delivery with 4T score calculation and cessation of heparin for patients with suspected HIT.



KEYWORDS
heparin, medical order entry systems, quality improvement, thrombocytopenia

Essentials

- Heparin-induced thrombocytopenia (HIT) is difficult to diagnose and to manage.
- Electronic medical record alerts improved clinical care of patients with suspected HIT.
- The alert recommending heparin discontinuation when HIT was suspected was successful.
- Electronic medical record interventions led to improvement in diagnosis and treatment of suspected HIT.

1 | INTRODUCTION

Heparin-induced thrombocytopenia (HIT) is a complex clinicopathologic syndrome that is difficult to diagnose and treat; if unrecognized, the associated mortality is 20% to 30% [1]. To assist clinicians, algorithms have been developed, as demonstrated in a recent illustrated review [2]. The first step is calculating the 4T score to determine pretest probability of HIT. If the 4T score is >3, testing with an immunoassay for antibodies to heparin-platelet factor 4 (PF4), discontinuing heparin, and starting a nonheparin anticoagulant are recommended. Confirmatory functional assays (eg, serotonin release assay and heparin-induced platelet aggregation assay) can be used when the immunoassay is positive, although patients with high probability 4T scores and strongly positive immunoassays may not require a confirmatory functional assay [3]. At our institution, for cost-saving purposes, a serotonin release assay is not routinely sent when the 4T score and heparin-PF4 enzyme-linked immunosorbent assay (ELISA) optical density are both high. The pretest probabilities are 0.2% for low probability (4T score, 0-3), 14% for intermediate probability (4-5), and 64% for high probability (6-8) [4]. If there is a high likelihood of HIT, the first critical management step is to discontinue heparin products, even before test results are available, and to start a nonheparin anticoagulant such as direct thrombin inhibitors (DTIs) or direct oral anticoagulant to avoid morbidity and mortality. Sending tests when the clinical suspicion is low or as a "rule out" is inappropriate and can lead to increased cost, unnecessary use of expensive nonheparin anticoagulants, and overdiagnosis.

The Hemostatic and Antithrombotic (HAT) Stewardship team at Brigham and Women's Hospital supports all inpatient services in the management of patients with suspected or confirmed HIT [5]. During internal quality reviews, we found that providers were not calculating or documenting 4T scores, heparin-PF4 tests were sent inappropriately, and heparin products were not stopped despite ordering heparin-PF4 tests. As part of ongoing quality improvement initiatives, the HAT Stewardship and the Clinical Decision Support teams worked together on electronic health record (EHR)-based interventions to change practice and improve patient safety. Three interruptive interventions were embedded at the point-of-care when heparin-PF4 test ordering occurred to improve the safety and management of patients with suspected HIT. The aim of this study was to assess the impact of these 3 interruptive alerts on the care of patients with suspected HIT.

2 | METHODS

Three interventions were built in the EHR (Epic Systems Inc) at Brigham and Women's Hospital, a 750-bed academic medical center in

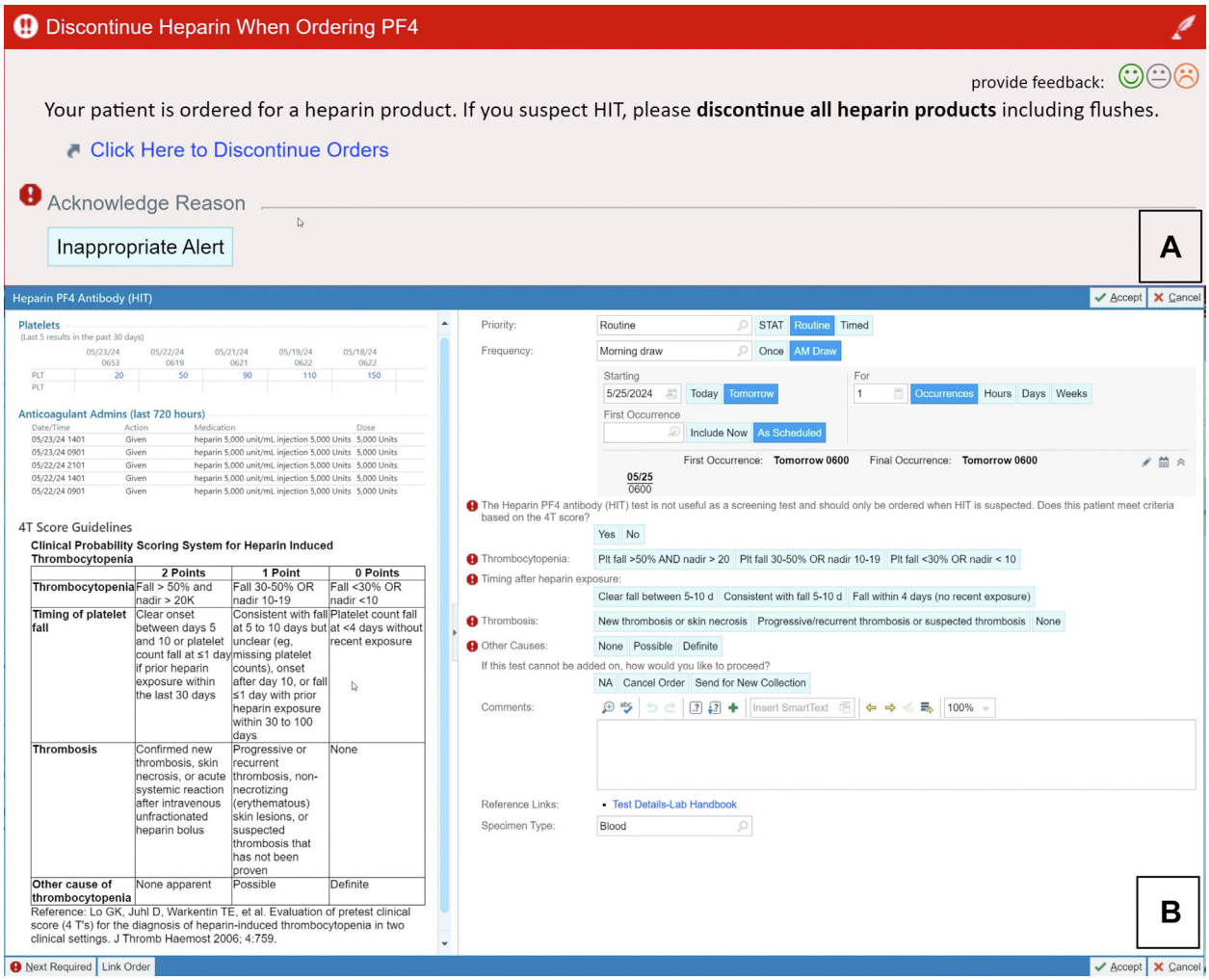


FIGURE 1 (A) Electronic health alert recommending discontinuation of heparin products when ordering a platelet factor 4 (PF4) test. (B) Heparin-PF4 test order. HIT, heparin-induced thrombocytopenia; Plt, platelet.

Boston, Massachusetts. This study received institutional review board approval.

2.1 | Intervention 1: alerting providers to discontinue heparin orders while awaiting heparin-PF4 test results

In December 2018, an interruptive alert was displayed to providers when ordering an immunoglobulin G–specific heparin-PF4 ELISA test (Immucor) for patients with active heparin orders. The alert (Figure 1A) recommended discontinuing all heparin products with a direct link to order entry to allow for discontinuation.

To analyze the effectiveness of this intervention, all heparin-PF4 test orders in 12 months prior ("Pre") and 12 months after ("Post") alert implementation were evaluated. Each test was assessed to determine if heparin was administered between the time of ordering the heparin-PF4 test and the time of receiving the test result. Eligible heparin-PF4 orders were those that were signed, had active heparin orders at the time of heparin-PF4 testing, and had blood samples sent to the laboratory.

2.2 | Intervention 2: increasing appropriateness of heparin-PF4 testing

In August 2020, an intervention to increase appropriate heparin-PF4 test ordering was implemented, requiring providers to assess pretest probability of HIT by documenting the 4T score elements. Appropriate heparin-PF4 ordering was defined as the 4T score of >3. Effectiveness was assessed by comparing the 4T scores associated with heparin-PF4 tests for a period of 9 months before and after this intervention went live. In the Pre time period, if no 4T score was in the EHR, 2 HAT Stewardship team members (1 PharmD and 1 trainee), blinded to heparin-PF4 results, retrospectively calculated the 4T score using a

comprehensive rubric. Discrepant scores were adjudicated by the HAT Stewardship PharmD manager. After implementation of intervention 2, 4T scores were required to sign the heparin-PF4 test order. Due to EHR limitations, the aggregate 4T score was not automatically calculated, but the clinical information on 4T scoring was displayed (Figure 1B).

2.3 | Intervention 3: alerting providers ordering inappropriate heparin-PF4 tests

During the same time period as intervention 2, an interruptive alert was displayed, informing providers before signing the heparin-PF4 test order that the 4T score was <4. This randomized alert was only shown to providers with an odd provider identification number to allow assessment of the effectiveness of the intervention. Orders that were initiated but not signed were not included in our analysis.

All data were extracted from the EHR using SQL (Oracle Corporation) and analyzed in Python (Python Software Foundation). Chi-squared analysis was used to determine statistical significance between the groups.

3 | RESULTS AND DISCUSSION

Despite available international [3] and institutional guidelines on how to diagnose and manage HIT, best practices were not routinely followed at our institution. These quality improvement interventions embedded in the EHR were designed to address these practice gaps. The implementation of these interventions resulted in improved management and patient safety in cases of suspected HIT.

The first interruptive alert, intervention 1, to discontinue heparin if HIT was suspected, resulted in an 11% decrease in inappropriate heparin continuation, from 65% (191 heparin orders/293 heparin-PF4 ELISA tests) of cases inappropriately continuing heparin preinterruptive alert to 54% (127 heparin orders/235 heparin-PF4 ELISA tests) cases continuing heparin postinterruptive alert (P = .02). This alert was the most successful electronic intervention at our institution, likely due to the clarity of the request and inability to move forward without acknowledging the alert and reason for override. This alert improved patient safety for the first critical step in the management of HIT. Further refinement of the alert linking heparin discontinuation with nonheparin anticoagulation initiation is in process as both treatment steps are critical. Currently, it is standard practice at our institution for providers to contact the HAT Stewardship team or Hematology consult service to discuss nonheparin anticoagulant management in cases of suspected HIT. Intravenous DTI use requires approval by the HAT Stewardship, Hematology, Vascular Medicine, or Interventional Cardiology. The HAT Stewardship team also regularly monitors heparin-PF4 test results and is available to assist clinicians to order alternative nonheparin anticoagulants.

Intervention 2 was designed to assist clinicians by identifying patients with high and low pretest probabilities of HIT by forcing calculation of the 4T score. In the preintervention group, only 31% (85 documented 4T scores/272 heparin-PF4 ELISA tests) of patients had a 4T score documented in the EHR. Of those in the preimplementation group with documented 4T scores, 69.4% (59/85) of ordered heparin-PF4 tests were determined to be appropriate with 4T scores of >3. Of those without documented 4T scores, the HAT research team found that only 27.2% had a 4T score of >3 (51/187). Overall, in the preintervention cohort, a composite of 40.4% ([59 + 51] / [85 + 187] = 110/272) of heparin-PF4 tests were ordered appropriately with a 4T score of >3. Given the risk of false positive heparin-PF4 results, tests sent for low 4T scores can lead to unnecessary additional testing, inappropriate use of expensive nonheparin anticoagulants, and increased economic burden [5]. Due to the design of intervention 2, 100% (311/311) of patients in the postintervention group had a documented 4T score, with 79.1% (246/311) ordered for appropriate 4T scores. This intervention increased appropriate heparin-PF4 test ordering from 40.4% to 79.1% ($P < .00001$), a nearly 40% statistically significant improvement in appropriate testing. Although it is possible that some clinicians intentionally entered false values to game the system, a concern shared by others [6], there were no punitive actions taken if a heparin-PF4 test was ordered despite the alert. The percentage of inappropriate tests was similar across multiple large services—surgical intensive care unit (32.3%), oncology ward (25.6%), cardiac critical care unit (24.5%), and adult medicine (23.8%; Figure 2).

We tested whether an additional targeted intervention could further improve management by decreasing the number of tests ordered when the 4T score was low to avoid overdiagnosis. Intervention 3, which randomized providers to see a recommendation not to order heparin-PF4 tests when the 4T score was <4, did not change clinical practice. The percent of inappropriate heparin-PF4 test orders was not different between the control group providers and those exposed to intervention 3 (96 inappropriate orders/402 total orders, 24% in the control group, vs 56 inappropriate orders/298 total orders, 19% in the test group; P = .13). In the intervention group, there were 364 unique providers ordering heparin-PF4 tests, and 53% were residents. Additionally, the median number of tests ordered per provider was 1 (IQR, 1-2), making it unlikely that each provider learned from seeing this alert to affect subsequent heparin-PF4 test ordering practice. Although we found a trend toward decreased inappropriate ordering, it was not statistically significant. One reason for this may be that it is often difficult to determine the etiology of thrombocytopenia in critical care patients, resulting in continued inappropriate heparin-PF4 test ordering, especially by services such as the cardiac critical care unit and surgical intensive care unit, which more frequently use therapeutic dose unfractionated heparin. Therapeutic heparin dosing is associated with an increased risk of HIT compared with prophylaxis [7], which may increase a provider's concern for HIT, regardless of 4T score.

Although other electronic clinical decision tools to aid in the diagnosis and management of HIT have been reported, they have had limited success and have focused on diagnostic testing, not clinical management, alerts. Studies evaluating electronic systems to help identify potential cases of HIT have found that while more HIT

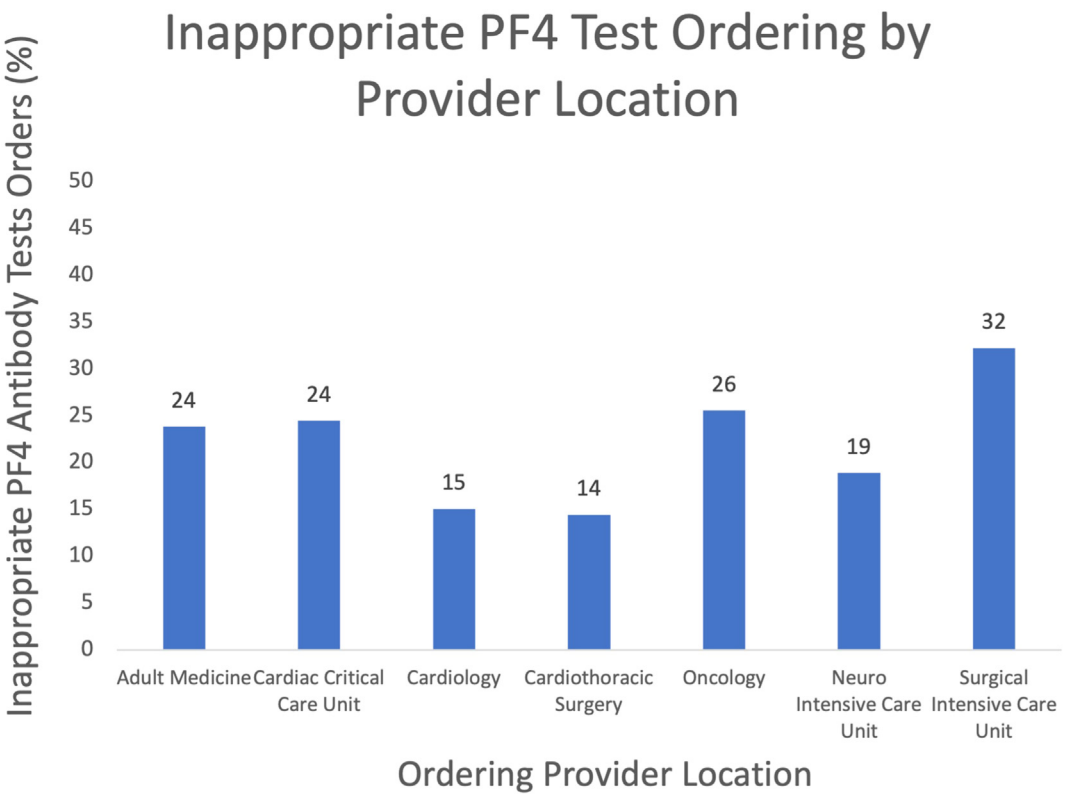


FIGURE 2 Inappropriate platelet factor 4 (PF4) ordering by provider location. $P = .13$.

testing is performed, inappropriate HIT testing patterns often result [8–12]. One study of a computer-based order entry intervention to calculate the 4T score before ordering tests for HIT found a nonsignificant trend in a reduction of inappropriate testing of those with low 4T scores, unlike our interruptive alert 2, which resulted in a significant 38.7% decrease in inappropriate testing [13]. Another study implemented a paper 4T scoring form and required consultation from a dedicated anticoagulation service before test ordering; while this led to a decrease in immunoassay and functional assays for HIT by 37.5% and 85%, respectively, soon after initiation, it required regular follow-up and close hematology and pharmacy management as it was not an electronically driven intervention [14]. Although improvement of documentation of 4T scores and/or heparin-PF4 testing has sometimes been reported, heparin discontinuation and use of appropriate nonheparin anticoagulation following these assessments are critical. One study that used an interruptive alert to notify clinicians of new thrombocytopenia in the setting of heparin exposure showed an increase in HIT antibody testing, while heparin discontinuation only improved by 5% (21.2%-26.5%) [10]. Our innovative heparin discontinuation alert improved discontinuation of heparin products by 11%. Electronic alerts and anticoagulation stewardship programs are complementary, with electronic health alerts helping to reduce the burden on the hematologists and pharmacists. These health alerts can be combined with provider education regarding the risks of inappropriate HIT management to further improve treatment of this life-threatening diagnosis. The interventions used in these initiatives can be implemented at other institutions to aid diagnostic and treatment protocols for patients with suspected HIT.

Limitations include some retrospective components and a single-center large academic institution analysis. For each assessment, we evaluated only signed heparin-PF4 test orders and may have missed critical decision-making by clinicians who decided not to order the test, although the low rate of 4T score documentation and heparin-PF4 test order appropriateness argues against this. Provider feedback on these interruptive alerts was not formally obtained, although the education sessions were well received.

In conclusion, the use of these interruptive interventions embedded in the EHR at time of heparin-PF4 test ordering resulted in significant improvement in the diagnosis and management of suspected HIT at our institution. Specifically, these interruptive interventions led to improved guideline-based, accurate care delivery with an increase in 4T score calculation by providers and cessation of heparin for patients with suspected HIT. Further use of these interventions and the addition of an electronic alert for DTI management are ongoing to improve care of patients with suspected or acute HIT.

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AUTHOR CONTRIBUTIONS

Designed research: K.W.S., D.R., J.G., J.K., R.P., and J.M.C. Data collection: K.W.S., D.R., J.G., J.K., S.T., and M.A. Data analysis: R.L.Z., K.W.S, D.R., R.P., and J.M.C. Wrote paper: R.L.Z., K.W.S., D.R., R.P., and J.M.C.

RELATIONSHIP DISCLOSURE

R.L.Z.: consulting fees and stock in Amagma Inc and other financial contributions from Primum. K.W.S.: honoraria for AC Forum March 2022, ASHP Midyear 2022, and AC Forum Webinar July 2023. D.R.: consulting fees for Statera Health. J.G.: involved in the Anticoagulation Certificate program and Podcast on Medication Use Evaluation for ASHP. J.M.C.: consulting fees from Abbott, honoraria from Roche and Sanofi, and participation in Advisory Boards for Anthos, Bristol Myers Squibb, Werfen, and Pfizer. Council member for ISTH, Steering Committee Member for World Thrombosis Day, and Committee on Practice for American Society of Hematology. The following individuals have no conflict of interest to report: J.K., S.T., M.A., and R.P.

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