


# BMJ Open Quality Improving compliance with appropriateness of testing for heparin-induced thrombocytopenia: a quality improvement report

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## ABSTRACT

Heparin-induced thrombocytopenia (HIT) is a serious complication of heparin therapy. Evidence-based guidelines recommend the use of the 4Ts scoring system to calculate pretest probability of HIT. However, this scoring system is often underused, and inappropriate testing can lead to increased morbidity, medical costs and length of hospital stay. We identified that inappropriate testing for HIT was common at our institution and implemented structured multicomponent educational interventions to evaluate the impact of education on the appropriateness of HIT testing. The educational interventions led to a significantly increased rate of appropriateness of HIT testing (69% vs 35%;  $p=0.001$ ). In addition, the 4Ts score documentation rate significantly improved following the intervention (52% vs 17%;  $p=0.001$ ). The rates of discontinuation of heparin products and initiation of alternative anticoagulation increased, although not statistically significantly. Educational interventions can improve compliance with evidence-based guidelines on appropriateness of testing for HIT.

## INTRODUCTION

Thrombocytopenia acquired during hospitalisation is common with a reported incidence of up to 25%–50% in the intensive care unit setting.<sup>1</sup> Heparin-induced thrombocytopenia (HIT) is often suspected when there is an acute drop in the platelet count in patients receiving heparin products. HIT is associated with increased morbidity and mortality, and early diagnosis and treatment is critical.<sup>2</sup> The diagnosis of HIT can be challenging in hospitalised patients given the frequency of heparin use and the presence of numerous alternative causes of thrombocytopenia.

The evidence-based guidelines of the American Society of Hematology (ASH) recommend the use of the 4Ts score to calculate the pretest probability of HIT in suspected cases.<sup>3</sup> The 4Ts scoring system has been shown to have a high negative predictive value when a low-probability score is present.<sup>4</sup> In patients with low pretest probability for HIT, testing is

## WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Overtesting for heparin-induced thrombocytopenia (HIT) is common and associated with adverse clinical outcomes.

## WHAT THIS STUDY ADDS

⇒ This study highlights that quality improvement initiatives can effectively improve compliance with appropriateness of testing for HIT.

## HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ This quality improvement initiative provides evidence on using multifaceted educational interventions to achieve sustainable outcomes in compliance with evidence-based practice guidelines for HIT.

not only unnecessary, but also has the potential to cause harm due to prolonged length of hospital stay, increased costs and increased bleeding risk with the use of alternative anticoagulants.<sup>5,6</sup> Therefore, The ASH Choosing Wisely Campaign has advised providers not to test or treat for suspected HIT in patients with a pretest low-probability 4Ts score.<sup>7</sup>

Previous studies have shown that overtesting for HIT is common despite the evidence-based guidelines, leading to poor clinical outcomes and increased health-care expenditures.<sup>8–10</sup> Educational interventions for physicians have been shown to be successful in reducing inappropriate testing for HIT.<sup>11,12</sup> The aim of our quality improvement project was to quantify retrospectively the appropriateness of HIT testing in adults hospitalised on medical services at a teaching hospital, and examine the impact of a prospective educational campaign targeting medical residents on the practice of appropriate HIT testing, which may result in improved compliance with the evidence-based guidelines.

## METHODS

### Clinical setting and stakeholders

The quality improvement study was conducted at a teaching hospital (St. Elizabeth's Medical Center, Boston, Massachusetts, USA). In brief, this is a 273-bed acute care hospital in Boston that provides tertiary care for a large integrated healthcare system that operates nine hospitals in eastern Massachusetts (Steward Health Care System, Dallas, Texas, USA). During the conduct of the study, the hospital had an average of 15 930 admissions per year, with 75% on medical and surgical services. We used the Standards for Quality Improvement Reporting Excellence guidelines.<sup>13</sup> The stakeholders included 56 trainees representing our entire internal medicine residency programme, clinical pharmacists, and the hospital-based teaching faculty, including hospitalists, cardiologists, pulmonologists and critical care physicians.

### Baseline assessment of practice pattern for HIT testing

The quality improvement project was initiated in January 2018. In the first phase, we identified patients hospitalised on medical services (ie, general medicine, pulmonary, and cardiology service, and medical intensive care unit) who underwent testing for HIT, using the ELISA (Quest Diagnostics, San Juan Capistrano, California, USA) that detects heparin-PF4 antibodies, over a 12-month period (1 January 2018 to 1 January 2019). The primary source for the data was the hospital's electronic health record (MEDITECH, Westwood, Massachusetts, USA). The electronic health record was used to run a report to identify patients who underwent testing for HIT within the specified time frame.

The following deidentified data were collected from the patient's medical record: age, gender, heparin products, namely unfractionated heparin and low-molecular weight heparin (ie, enoxaparin), mode of administration (subcutaneous, intermittent intravenous injection or continuous infusion), major clinical diagnoses, and surgery in the prior 3 months.

### Outcome measures

The outcome measure of interest was the percentage of patients who underwent appropriate testing for HIT. Appropriate testing was defined as an ordered HIT immunological assay (ie, ELISA) in a patient with a pretest moderate to high probability of HIT based on the 4Ts scoring system, defined by a 4Ts score of 4 or more. The 4Ts score was calculated for each patient by two medical residents (MM, VK) and a clinical pharmacist (DN). Conflicts were resolved through consensus. The 4Ts scores were calculated in each case based on the information provided at the time testing was ordered. Additional outcomes of interest included documentation of the 4Ts score in the electronic health record by the primary team ordering the test, the percentage of patients in whom heparin products were discontinued and alternative agents (eg, argatroban, bivalirudin, fondaparinux or direct oral anticoagulants) were initiated, and the

percentage of patients in whom the haematology service was consulted.

### Description of the quality improvement plan and educational intervention

The second phase involved the planning and implementation of an intervention to encourage judicious laboratory testing for HIT, guided by the evidence-based practice guideline that recommends the use of the 4Ts clinical scoring system to determine the pretest probability of HIT in a patient before laboratory testing is performed. Our intervention was implemented in August 2019 and focused on education (figure 1). Using a multipronged approach, internal medicine residents, clinical pharmacists and attending physicians received education in small group settings in addition to a 1-hour lecture that was presented to medical residents. Educational sessions were conducted by three of the authors (MM, VK and DN). No incentives (such as monetary compensation or continuing education credits) were provided to participate in the educational sessions. Not all faculty, clinical pharmacists or medical residents were available during the educational sessions due to competing obligations. However, the attendance rate was above 80% across all stakeholders. Pocket cards summarising the ASH recommendations were distributed during small group sessions and via email (online supplemental file 1). In addition, educational materials were posted at workstations on the medical wards and in the intensive care unit. The educational sessions were incorporated into established didactic structure and the intervention did not require significant expenses. Following the intervention, over the ensuing 10 months (1 September 2019 to 1 July 2020), hospitalised patients receiving HIT testing were identified using the same aforementioned method.

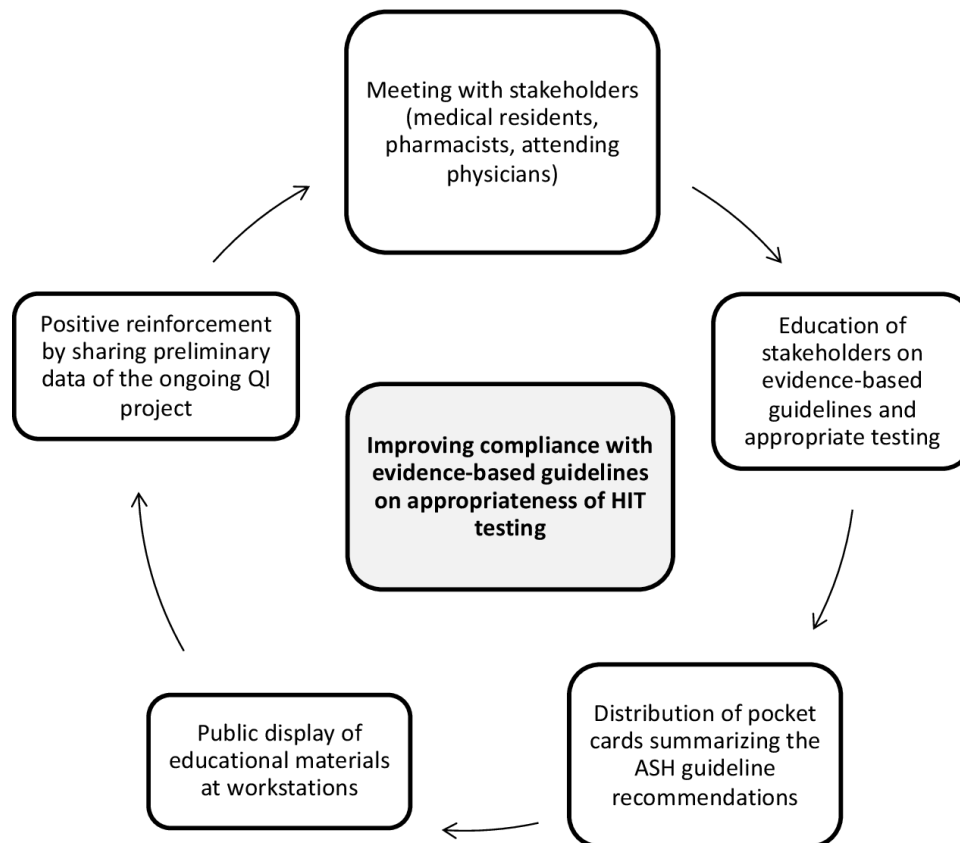
Continuous variables were reported as mean (with SD or SE of the mean), and binary variables were reported as counts (with percentage). Comparisons between groups were made by the Student's t-test for continuous variables and by the  $\chi^2$  test for categorical variables. All analyses were performed using Stata/MP V.14 for Mac (StataCorp). Differences were considered statistically significant at a  $p < 0.05$ .

Patients or the public were not involved in the design, conduct, reporting or dissemination plans of our project.

## RESULTS

### Baseline assessment of appropriateness of HIT testing

A total of 60 patients hospitalised on the medical wards and in the intensive care unit who received laboratory testing for HIT were identified in the baseline preintervention period. As shown in table 1, the mean age was 69 years, 57% were men, 65% were in the intensive care unit, 35% had sepsis, 28% had cardiac disease and 88% were receiving unfractionated heparin. As shown in table 2,



**Figure 1** Framework describing educational interventions to improve compliance with evidence-based guidelines on appropriateness of testing for heparin-induced thrombocytopenia (HIT). ASH, American Society of Hematology; QI, quality improvement.

the percentage of patients receiving appropriate testing for HIT, in accordance with the 4Ts scoring system, was only 35%. Documentation of the 4Ts score in the

medical record was only present in 17% of patients. The frequency of discontinuation of heparin products and the initiation of alternative anticoagulation was 65% and

**Table 1** Clinical characteristics of patients who underwent testing for HIT during the preintervention and postintervention period

	Preintervention period (n=60)	Postintervention period (n=42)	P value
Age, years	69±16	65±18	0.28
Men	28 (47%)	28 (67%)	0.05
Inpatient setting			0.94
General ward	21 (35%)	15 (36%)	
Intensive care unit	39 (65%)	27 (64%)	
Primary diagnosis			0.02
Sepsis	21 (35%)	11 (26%)	
Cardiac disease	17 (28%)	5 (12%)	
Venous thromboembolism	4 (7%)	2 (5%)	
Malignancy	5 (8%)	2 (5%)	
Other	13 (22%)	22 (52%)	
Surgery in the prior 3 months	8 (14%)	10 (24%)	0.19
Heparin product			0.08
Unfractionated heparin	53 (88%)	41 (98%)	
Low-molecular-weight heparin	7 (12%)	1 (2%)	

Data summarised as mean±SD for continuous variables or n (%) for categorical variables.

**Table 2** Impact of the intervention on the outcome measures of interest

Outcome measure	Preintervention period (n=60)	Postintervention period (n=42)	P value
Appropriateness of HIT testing, n (%)	21 (35)	29 (69)	0.001
4Ts scoring system documentation, n (%)	10 (17)	22 (52)	0.001
Discontinuation of heparin products, n (%)	39 (65)	34 (81)	0.08
Initiation of alternative anticoagulation, n (%)	13 (22)	15 (36)	0.12
Request for a haematology consult, n (%)	15 (25)	12 (29)	0.68

Data summarised as n (%) for categorical variables.  
HIT, heparin-induced thrombocytopenia.

22%, respectively. The haematology service was consulted in 25% of the cases.

### Postintervention assessment of appropriateness of HIT testing

Following the educational intervention, over the ensuing 10 months, we identified a total of 42 hospitalised patients who received testing for HIT. The mean age was 65 years, 67% were men, 65% were in the intensive care unit, 26% had sepsis, 12% had cardiac disease and 98% were receiving unfractionated heparin. The characteristics of these patients did not differ significantly from those identified in the baseline preintervention period except for gender and the major clinical diagnoses (table 1).

The results of the intervention are summarised in table 2. In brief, the appropriateness of HIT testing significantly improved in the postintervention period compared with the baseline assessment period (69% vs 35%;  $p=0.001$ ). Moreover, the 4Ts score documentation rate significantly improved in the postintervention period (52% vs 17%;  $p=0.001$ ). Although there was a non-significant trend toward an increase in the rate of discontinuation of heparin products in the postintervention period (81% vs 65%;  $p=0.08$ ), there was no significant increase in the initiation of alternative anticoagulation (36% vs 22%;  $p=0.12$ ). The percentage of haematology consults were comparable between the two periods ( $p=0.68$ ). The rate of inappropriate testing and initiation of alternative anticoagulation was not different among patients who did and did not receive a haematology consultation ( $p=0.09$  and 0.07, respectively).

Of note, our intervention had no significant impact on hospital length of stay, with a mean of 17.7 days in the preintervention period and 17.8 days in the postintervention period ( $p=0.97$ ). Among all 102 patients, there was also no significant difference in the hospital length of stay between those who received appropriate versus inappropriate testing for HIT (18.7 vs 16.8 days;  $p=0.50$ ). None of the patients with a low pretest probability for HIT during both the preintervention and postintervention period had confirmed HIT by a functional platelet-activation assay.

### DISCUSSION

Our education-focused quality improvement project led to significant improvement in the 4Ts score documentation (with an increase from 17% to 52%) and appropriateness of HIT testing (with an increased from 35% to 69%) in the postintervention compared with the baseline assessment period. There was no significant change in the rate of initiation of alternative anticoagulation or hospital length of stay.

In concordance with our results, prior studies have shown that HIT testing is overused. More than 100–150 immunological assays for HIT are performed annually at institutions for detection of circulating heparin-PF4 antibodies.<sup>11 14 15</sup> Inappropriate HIT testing is associated with increased hospital length of stay and healthcare costs, and can result in potential harm due to unnecessary anticoagulation in patients with low-pretest probability of the disease. In a retrospective study of 150 patients who were tested for HIT, the total estimated cost of both testing and use of anticoagulants was US\$238 180 over a 12-month period and only one patient tested positive for HIT.<sup>14</sup> The ASH Choosing Wisely guideline recommends the use of the 4Ts score to calculate the pretest probability of HIT in suspected cases as this scoring system has a high negative predictive value.<sup>16</sup> However, studies have shown that physician adherence to the 4Ts scoring system has not changed after the release of the ASH clinical practice guideline and the Choosing Wisely Campaign.<sup>8–10</sup>

Inappropriateness of HIT testing has ranged between 60% and 86% in previous studies investigating the impact of education.<sup>11 17</sup> Prior to our intervention, 65% of HIT testing at our institution was inappropriate, which is concordant with the literature. Based on this evidence, further efforts are required to improve compliance with the ASHs clinical practice guideline. Limited evidence shows that institutional educational interventions for healthcare providers can have a significant impact on reducing inappropriate HIT testing, although the data are conflicting.<sup>11 12 18</sup> In one study, education alone improved appropriateness of HIT testing from 14% to 37%, but did not have a significant impact on documentation of the 4Ts score.<sup>11</sup> In our study, our educational intervention improved 4Ts score documentation in addition to appropriateness of HIT testing. Our study further adds

that education may improve compliance with discontinuation of heparin products, although the difference was not statistically significant.

Implementation of decision support tools into electronic health records may have a potential role in increasing appropriateness of HIT testing.<sup>11</sup> Although educational interventions can have a short-term impact, there is limited long-term data available on effectiveness of education as the sole intervention. Therefore, decision support tools in addition to continuous educational interventions might be beneficial for long-term and sustained effects. In the next phase of our project, we plan to incorporate decision support tools into our hospital's computerised provider order set for HIT testing, with a forcing function, requiring the need to calculate the 4Ts score before ordering the immunological assay.

### Limitations

We acknowledge that our quality improvement project is limited by the small sample size and a single-centre intervention. Furthermore, given the fact that certain components of the 4Ts score may be subjective, inter-rater variability cannot be ruled out. To mitigate this limitation, any uncertainties were resolved by consensus between three authors. Additionally, the authors were not haematologists, which might have influenced the calculation of the 4Ts score. Our study was conducted in a teaching hospital that served as a tertiary care centre for our healthcare system, and non-medical patients were excluded. Although a common limitation to all quality improvement studies, the cohort of physicians and clinical pharmacists in the preintervention and postintervention period was not precisely matched, therefore, making it difficult to attribute observed outcomes solely to the intervention. Moreover, we primarily focused on the use of the immunological assay (ie, ELISA) to test for HIT, and did not evaluate the role of functional platelet-activation assays, such as the serotonin release assay. It is worth noting that in our study, patients who were tested for HIT had a prolonged hospital length of stay. This may be due in part to the high percentage of critically ill patients and the fact that testing for HIT was more likely to occur in sicker and more medically complex patients.

### CONCLUSIONS

Testing for HIT is frequently overused and inappropriate testing is associated with adverse healthcare outcomes. Our quality improvement initiative identified that inappropriate testing for HIT was common at our institution, concordant with the previous reports. Educational interventions can be low cost and successful approaches to reducing inappropriate HIT testing, although the published literature is very limited. Our multipronged educational intervention focusing on the ASH evidence-based guideline decreased the rate of inappropriate testing for HIT. The findings also suggest that these interventions can improve the compliance with other

evidence-based recommendations such as discontinuation of heparin products.

### IMPLICATIONS

Overall, this study contributes to knowledge on how to improve compliance with an evidence-based practice guideline for HIT. The findings demonstrate that multifaceted educational interventions improve compliance with evidence-based guidelines for HIT, including a significant reduction in inappropriate testing for HIT. Furthermore, our findings emphasise that education should be multifaceted and aimed at different healthcare providers, including attending physicians, resident physicians and clinical pharmacists. The results indicate that implementation of educational interventions have the potential to improve compliance with evidence-based guidelines on HIT and reduce morbidity. Future research is needed to explore the impact of educational interventions in different settings. The next step in our project is incorporation of decision support tools into our hospital's computerised provider order set for HIT testing to aid in calculating the 4Ts score and decision making on ordering the screening immunological assay.

**Contributors** MM, VK and DN performed chart review and 4T score calculations. VK, MM, DN and AU developed educational lectures, workshops and handouts. Data analysis was done by MM and BJ. All authors participated in QI project design. Manuscript was written by MM, VK and DN, all authors reviewed and edited the manuscript. BLJ is responsible for the overall content of the manuscript as the guarantor.

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## REFERENCES

- 1 Ali N, Auerbach HE. New-Onset acute thrombocytopenia in hospitalized patients: pathophysiology and diagnostic approach. *J Community Hosp Intern Med Perspect* 2017;7:157–67.
- 2 Franchini M. Heparin-Induced thrombocytopenia: an update. *Thromb J* 2005;3:14.
- 3 Cuker A, Arepally GM, Chong BH, et al. American Society of hematology 2018 guidelines for management of venous thromboembolism: heparin-induced thrombocytopenia. *Blood Adv* 2018;2:3360–92.
- 4 Lo GK, Juhl D, Warkentin TE, et al. Evaluation of pretest clinical score (4 T's) for the diagnosis of heparin-induced thrombocytopenia in two clinical settings. *J Thromb Haemost* 2006;4:759–65.
- 5 Rice L. Hits and misses in 100 years of heparin. *Hematology Am Soc Hematol Educ Program* 2017;2017:667–73.
- 6 Potdar R, Gupta S, Ng JH, et al. Utilizing the predictive value of the 4T scoring system to reduce unnecessary hit panel costs in the community hospital setting. *Blood* 2018;132:5001.
- 7 Hilal T, Munoz J. Choosing Wisely® in hematology: have we made a difference? *Curr Hematol Malig Rep* 2020;15:241–7.
- 8 Li A, Hicks LK, Fan E. Things we do for no reason: hit testing in low probability patients. *J Hosp Med* 2019;14:374–6.
- 9 Landau DA, Kholodnaya N, CuestaFernandez A, et al. The appropriateness of heparin antibody testing. A single institution retrospective analysis. *Blood* 2015;126:3277.
- 10 Baranwal A, Joseph S, Quality JS. Quality and Value-Focused Decision Making in Heparin-Induced Thrombocytopenia: The Impact of the American Society of Hematology's Choosing Wisely Initiative. *Blood* 2016;128:2342.
- 11 Arshad A, Alnimer L, Samhoury Y, et al. Impact of education and electronic decision support tool on the practice of heparin-induced thrombocytopenia testing: an experience of a teaching community hospital. *Thromb Res* 2018;169:73–5.
- 12 Lim MY, Foster J, Rourk A, et al. Initial and long term impact of a multi-disciplinary Task force in the diagnosis and management of heparin-induced thrombocytopenia. *J Thromb Thrombolysis* 2018;45:130–4.
- 13 Ogrinc G, Mooney SE, Estrada C, et al. The Squire (standards for quality improvement reporting excellence) guidelines for quality improvement reporting: explanation and elaboration. *Qual Saf Health Care* 2008;17 Suppl 1:i13–32.
- 14 Goldman R, Ustun B, Levine RL. Retrospective cost analysis of testing for hit antibodies in a community hospital. *Blood* 2008;112:4544.
- 15 Xavier M. Retrospective analysis of heparin-induced thrombocytopenia management at a large tertiary hospital. *J Hematol* 2014;3:27–33.
- 16 Hicks LK, Bering H, Carson KR, et al. Five hematologic tests and treatments to question. *Blood* 2014;124:3524–8.
- 17 Namakydoust A, Saha D, Ajeti G, et al. Appropriateness of testing for heparin-induced thrombocytopenia in hospitalized patients. *Journal of Clinical Oncology* 2016;34:252.
- 18 Malalur P, Greenberg C, Lim MY. Limited impact of clinician education on reducing inappropriate PF4 testing for heparin-induced thrombocytopenia. *J Thromb Thrombolysis* 2019;47:287–91.