Validation of the heparin-induced thrombocytopenia diagnosis code using a large-scale electronic health record database

EPH39

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BACKGROUND

Heparin-induced thrombocytopenia (HIT) is a life-threatening condition suspected in patients with new onset thrombocytopenia after exposure to heparin. However, laboratory testing to confirm HIT can be time-consuming and patients may carry a suspected diagnosis in their medical record for an extended period.

OBJECTIVE

The objective of this study was to evaluate the performance of the ICD-10-CM diagnosis code for HIT against lab-validated results in a large-scale electronic health record (EHR) database.

METHODS

This was a retrospective, observational cohort study of adult patients aged 18 years or older in the TriNetX Dataworks-USA research network of de-identified EHR data with an incident HIT diagnosis (ICD-10-CM code D75.82) (index date) from 01 Jan 2018 to 31 Dec 2024. Patients were required to have at least one year of baseline history and were followed for up to 42 days after the index date. Lab-confirmed HIT was determined based on an ELISA optical density (OD) ≥2.0 and/or a positive serotonin release assay (SRA) or heparin-induced platelet aggregation assay. The sensitivity, specificity, and positive predictive value (PPV) of the ICD-10-CM diagnosis code for HIT was estimated.

Demographics, baseline clinical characteristics, exposures, and treatments were described for true positives, false positives, and false negatives and effect size was estimated by Cohen's *d*/Cohen's *h*, with values less than 0.2 interpreted as a small difference between true positives and other groups.

ABBREVIATIONS
AI=American Indian; AN=Alaska Native; DOAC=direct oral anticoagulant; EHR=electronic health record; ELISA=enzyme-linked immunosorbent assay; HIT=heparin-induced thrombocytopenia; ICD-10-CM=International Classification of Diseases, 10th Revision, Clinical Modification; NH=Native Hawaiian; OD=optical density PI=Pacific Islander; PPV=positive predictive value; SD=standard deviation; SRA=serotonin release assay; UFH=unfractionated heparin

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RESULTS

- A total of 8,537 patients had at least one ICD-10-CM diagnosis code for HIT. Of the patients with a diagnosis code, 1,803 were true positives and 6,734 were false positives. There were 3,137 false negatives in the dataset (Figure 1).
- Performance of the code included an estimated 36.5% sensitivity, 99.99% specificity, and 21.1% PPV (Figure 1).
- As further restrictions were applied, the PPV increased to 30.9% (≥1 inpatient code) and 34.4% (≥2 codes between 2 and 14 days apart) (Figure 1).
- Patients who were true positives were more likely to have recent unfractionated heparin (UFH) exposure (*h*: 0.33-0.50) and be treated with a non-heparin anticoagulant (e.g., argatroban [*h*: 0.20-0.45], bivalirudin [*h*: 0.46-0.60], fondaparinux [*h*: 0.21-0.32]) after diagnosis (Table 2).

Table 1. Baseline patient demographics

	True positives N=1803	False positives N=6734	*d/h*	False negatives N=3137	*d/h*
Age at index					
Mean (SD)	62.6 (13.7)	62.7 (14.1)	0.01	62.3 (14.0)	0.02
Sex, n (%)					
Female	843 (46.8)	3204 (47.6)	0.02	1548 (49.3)	0.05
Male	959 (53.2)	3524 (52.3)	0.02	1587 (50.6)	0.05
Unknown	≤10 (≤0.6)	≤10 (≤0.1)	0.07	≤10 (≤0.3)	0.04
Race, n (%)					
Black	320 (17.7)	1177 (17.5)	0.01	867 (27.6)	**0.24**
White	1286 (71.3)	4928 (73.2)	0.04	1787 (57.0)	**0.30**
Asian	67 (3.7)	129 (1.9)	0.11	147 (4.7)	0.05
NH/PI	24 (1.3)	41 (0.6)	0.08	47 (1.5)	0.01
AI/AN	≤10 (≤0.6)	36 (0.5)	0.00	13 (0.4)	0.02
Other	44 (2.4)	188 (2.8)	0.02	141 (4.5)	0.11
Unknown	53 (2.9)	235 (3.5)	0.03	135 (4.3)	0.07
Ethnicity, n (%)					
Hispanic or Latino	106 (5.9)	422 (6.3)	0.02	165 (5.3)	0.03
Not Hispanic or Latino	1567 (86.9)	5285 (78.5)	**0.22**	2629 (83.8)	0.09
Unknown	130 (7.2)	1027 (15.3)	**0.26**	343 (10.9)	0.13

Figure 1. Performance metrics of the ICD-10-CM D75.82 code for HIT

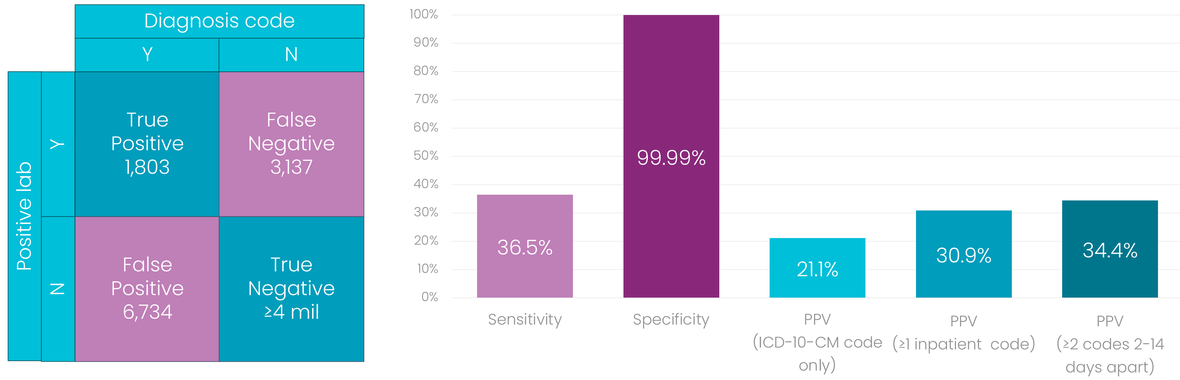

Table 2. Patient clinical characteristics

	True positives N=1803	False positives N=6734	*d/h*	False negatives N=3137	*d/h*
Comorbidities/risk factors					
ESRD/dialysis-dependent	253 (14.0)	1130 (16.8)	0.08	600 (19.1)	0.14
Major surgery	1490 (82.6)	5213 (77.4)	0.13	2372 (75.6)	0.17
Pregnancy/childbirth	24 (1.3)	90 (1.3)	0.00	46 (1.5)	0.01
Primary hypercoagulable states	136 (7.5)	473 (7.0)	0.02	168 (5.4)	0.09
Metastatic cancer	427 (23.7)	1367 (20.3)	0.08	743 (23.7)	0.00
Obesity	1302 (72.2)	4802 (71.3)	0.02	1691 (53.9)	**0.38**
Congestive heart failure	937 (52.0)	3033 (45.0)	0.14	1130 (36.0)	**0.32**
Systemic lupus erythematosus	18 (1.0)	149 (2.2)	0.10	73 (2.3)	0.11
Exposures, n (%)					
Unfractionated heparin (UFH)	1273 (70.6)	3105 (46.1)	**0.50**	2449 (78.1)	0.17
Enoxaparin	322 (17.9)	1225 (18.2)	0.01	906 (28.9)	**0.26**
Dalteparin	≤10 (≤0.6)	≤10 (≤0.1)	0.07	0 (0.0)	0.15
Treatments, n (%)					
Argatroban	678 (37.6)	1198 (17.8)	**0.45**	268 (8.5)	**0.73**
Bivalirudin	767 (42.5)	1068 (15.9)	**0.60**	410 (13.1)	**0.68**
Fondaparinux	442 (24.5)	822 (12.2)	**0.32**	294 (9.4)	**0.41**
Direct oral anticoagulants (DOAC)	894 (49.6)	1999 (29.7)	**0.41**	654 (20.8)	**0.61**

CONCLUSION

This study used a diagnostically complex condition to highlight the importance of using laboratory-confirmed diagnosis codes in pharmacoepidemiology studies, particularly for conditions with low prevalence, as the predictive value of the diagnosis code itself did not reliably predict HIT. The results of this study highlight key variables to consider (e.g., UFH exposure, treatment with non-heparin anticoagulants) for future work to develop a computable phenotype to more reliably define and identify HIT in pharmacoepidemiology studies.

LIMITATIONS

Laboratory antibody testing to confirm HIT is often performed outside of the hospital system and results may not be incorporated back into the structured EHR; as such, not all patients had lab testing to confirm or deny HIT. ELISA testing is not confirmatory for HIT; however, an OD over 2.0 strongly suggests HIT and was considered a true positive in this study. Due to constraints on the TriNetX LIVE™ platform, a positive SRA was only determined by ≥20% release in low UFH (0.1 U/mL) and not confirmed in high (100 U/mL) UFH concentrations.

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