Sequential combinations of rapid immunoassays for prompt recognition of heparin-induced thrombocytopenia: a prospective validation study

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BACKGROUND

- Early recognition and treatment of heparin-induced thrombocytopenia (HIT) are key to prevent severe complications
- Several rapid immunoassays are available for a rapid diagnosis of HIT, but sensitivity and specificity are not optimal
- Recent research has shown that:
  - Sequential combinations of multiple rapid immunoassays could improve the diagnostic work-up's accuracy[1,2]
  - New recently developed algorithms using multiple clinical and laboratory values, like the *« TORADI-HIT » algorithm*[3], can also improve diagnostic performances of rapid immunoassays

AIM

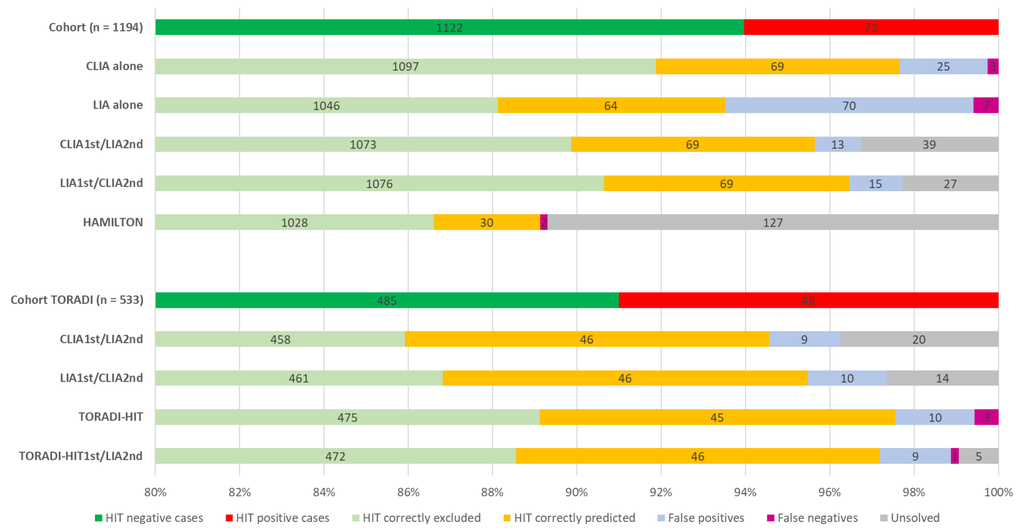
- To validate our two HIT-diagnostic Bayesian approaches associating 4T score and two sequentially performed rapid immunoassays
- To compare the performances of these two Bayesian approaches and two other HIT-diagnostic algorithms ("Hamilton"[4] based on two simultaneously performed immunoassays and "TORADI-HIT" [3] based on one immunoassay and other laboratory values)

CONCLUSION

Our diagnostic Bayesian approaches sequentially employing two IA are accurate for HIT diagnosis. Performing immunoassays simultaneously according to the "Hamilton algorithm" is less accurate, and more time and cost consuming. The TORADI-HIT algorithm offers better HIT exclusion at the cost of about 6% false negative results. Using our approaches, HIT exclusion or recognition can be achieved in >95% of cases within <1 hour with no false-negative results.

RESULTS

- Using CLIA first and LIA for unsolved cases correctly excluded HIT in **95.6%** and predicted HIT in **95.8%** (3.3% undetermined, 13 false positive, no false negative results)
- Using LIA first and CLIA for unsolved cases correctly excluded HIT in **96.4%** and predicted HIT in **97.2%** (2.3% undetermined, 15 false positive, no false negative results)
- TORADI-HIT[3] algorithm correctly excluded HIT in **97.9%** and predicted HIT in **93.8%** (0% undetermined, 10 false positive, **3 false negative results**)
- Hamilton[4] algorithm correctly excluded HIT in **92.1%** and predicted HIT in **42.3%** (10.7% undetermined, no false positive, **2 false negative results**)



	Sensitivity	Specificity	PPV	NPV
CLIA[1st]/LIA[2nd]	95.8%	95.6%	84.1%	100.0%
LIA[1st]/CLIA[2nd]	97.2%	96.4%	82.1%	100.0%
Hamilton	42.3%	92.1%	100.0%	99.8%
TORADI-HIT	93.8%	97.9%	81.8%	99.4%

PPV, positive predictive value; NPV, negative predictive value

METHOD

- Prospectively enrolled cohort of **1194 cases** with suspicion of HIT (6.0% confirmed HIT) for which rapid IAs were performed from 09.2020 to 04.2024
- For each case, CLIA (chemiluminescence-based immunoassay; Instrumentation Laboratory, Munich, Germany) and LIA (latex immune-turbidimetric assay; Instrumentation Laboratory) were performed in our laboratory
- Definite HIT confirmation or exclusion was made using heparin-induced platelet activation (HIPA) test and PF4-enhanced HIPA (PIPA)
- Following approaches were compared:
  1) **CLIA[1st]/LIA[2nd]**: 4T score combined with CLIA result (U/mL) predict or exclude HIT in most cases; for the remaining cases (grey-zone), LIA is performed as second-line[2]
  2) **LIA[1st]/CLIA[2nd]**: 4T score combined with LIA result (U/mL) predict or exclude HIT in most cases; for the remaining cases (grey-zone), CLIA is performed as second-line[2]
  3) **TORADI-HIT with CLIA**: CLIA result (U/mL) is combined with multiple clinical and laboratory data to obtain a post-test probability of HIT[3]
  4) **HAMILTON**: CLIA and LIA are performed simultaneously and a scoring system based on immunoassay results (U/mL) predicts or excludes HIT[4]

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