

Diagnostica di laboratorio in emostasi e trombosi

BEYOND POSITIVITY: THE HIERARCHICAL ROLE OF IMMUNOASSAYS IN HEPARIN INDUCED THROMBOCYTOPENIA

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Background and aims. Heparin induced thrombocytopenia (HIT) is an immune mediated disorder induced by the exposure to heparin with subsequent production of antibodies against heparin-platelet factor 4 (H-PF4) complexes. The diagnosis of HIT is based on a combination of 4T pre-test probability score (4Tscore) and detection of antibodies bound to H-PF4 complexes by immunoassays and, if available, a functional assay. Immunoassays are characterised by ease of performance, wide availability and high sensitivity. Functional assays are the gold standard for HIT diagnosis but these methods are complex, completely manual, requiring washed platelets and more expensive. This analysis aims to investigate the hierarchical role of immunoassays and their integration with the 4Ts score for ruling out HIT.

Methods. We conducted a retrospective analysis, from 2020 to 2026, of 103 patients from Azienda Ospedaliera Molinette with suspected HIT. For each case, the pre-test clinical probability was assessed using the 4Ts score. Laboratory evaluation included immunoassays (ELISA, CLIA, and LIA) and a functional assay (HIPA), used as the reference standard. Agreement between assays was evaluated using concordance rates, and diagnostic performance was assessed by calculating positive predictive value (PPV) and negative predictive value (NPV).

Results. 33 patients out of 103 (32%) were positive to immunoassays. HIPA was performed on only 9 patients; for the remaining 24 patients, it was not possible to carry out HIPA due to a lack of sufficient samples. In the group of 24 patients, clinical management was based solely on the immunoassays results. In the group of 9 patients, the distribution of 4Ts scores showed a predominance of intermediate-risk cases (7), with some patients classified as high probability (2). In the same group Immunoassays demonstrated a higher rate of positivity compared to the functional assay (ELISA 100%, CLIA 78%, LIA 89%), with HIPA positive in approximately half of the cases (67%). Concordance with HIPA was highest for CLIA (88.9%), followed by ELISA and LIA (both 66.7%). CLIA showed a high PPV (85,7%) and a NPV 100%, indicating strong rule-out capability. In contrast, ELISA and LIA showed lower reliability in excluding HIT, with NPV values of 0%.

Conclusions. The results suggest a hierarchical role among immunoassays in HIT diagnosis, with variable diagnostic performance. The integration of immunoassays with an intermediate-to-high 4Ts score may support exclusion of HIT, potentially reducing the need for functional testing. However, functional assays remain essential in cases with discordant or uncertain results.

Comparison	Simple Accordance	Cohen's kappa (k)	Result
ELISA vs HIPA	66,70%	0	absence of variance in the ELISA
CLIA vs HIPA	88,90%	0,73	a real and strong agreement
LIA vs HIPA	66,70%	-0,12	systematic disagreement