

Sindrome da anticorpi antifosfolipidi

OPTIMIZING CUT-OFFS FOR LUPUS ANTICOAGULANT TESTING: EVIDENCE FROM A MULTICENTER REGIONAL STUDY

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Background. Antiphospholipid syndrome requires a multidisciplinary approach, and despite similar analytical platforms across Tuscany, harmonization is needed to ensure diagnostic consistency. Accurate lupus anticoagulant (LAC) testing depends on minimizing clinical and laboratory variability, including standardized diagnostic algorithms, normalization methods, cut-off definition, and interpretative criteria. In this context, a regional working group was established in Tuscany in 2025 to promote harmonization of LAC testing and management.

Aims. To identify and compare optimal cut-offs for the LAC diagnostic algorithm using data from the Tuscany Regional Working Group on Hemostasis and Thrombosis.

Methods. Citrated plasma samples were collected from blood donors at hospital and university transfusion centers across Tuscany (October–December 2025). Donors were not on anticoagulant therapy and had no known atherothrombotic or autoimmune diseases. Samples were tested using a standardized LAC panel, including Silica Clotting Time (SCT) and Dilute Russell's Viper Venom Time (dRVVT) assays (screening, mixing, confirmatory) (Werfen, Italy). Analyses were performed on ACL TOP analyzers (Werfen, Italy). Results were expressed as ratios normalized to normal pooled plasma (NPP). Cut-offs were defined as the 99th percentile according to ISTH guidelines. Outliers were identified using CLSI criteria (values >1.5×IQR).

Results. A total of 198 samples (110 males, 88 females; mean age 42 years) were analyzed. Initial cut-offs (99th percentile) were: SCT screening 1.20, SCT mixing 1.10, SCT NTR 1.23; dRVVT screening 1.23, mixing 1.14, NTR 1.22. After exclusion of 9 outliers, SCT cut-offs remained unchanged, whereas dRVVT screening and NTR slightly decreased (1.19 and 1.21, respectively). In 98 AF patients from Careggi University Hospital, LAC positivity using previous (>1.2) and study-derived cut-offs showed 92.9% concordance (91/98) and 7.2% discordance, with excellent agreement (κ=0.85, $p<0.001$). No significant differences in clinical-laboratory characteristics were observed, except for lower anti-β2GPI IgG levels in discordant cases.

Conclusions. LAC standardization remains challenging, with the mixing test representing a critical step influenced by NPP quality. Standardized reference materials and collaborative initiatives may reduce variability, improve reproducibility, and enhance harmonization of LAC diagnostics.