

Clinical Utility of a Novel Screening Assay for the Detection of IgG and IgM Antibodies to the Phosphatidylserine/Prothrombin Complex

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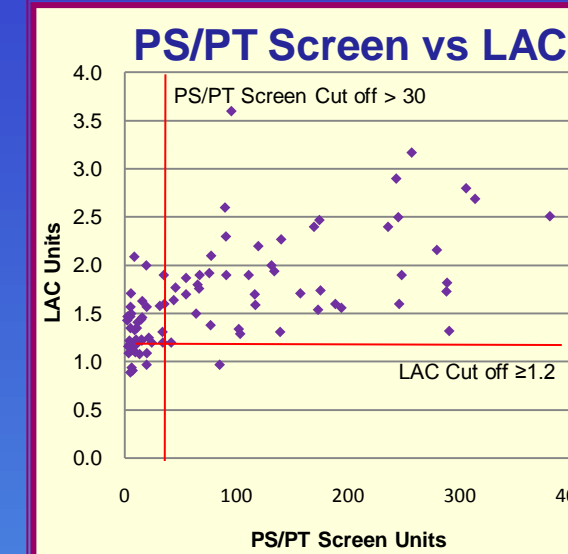
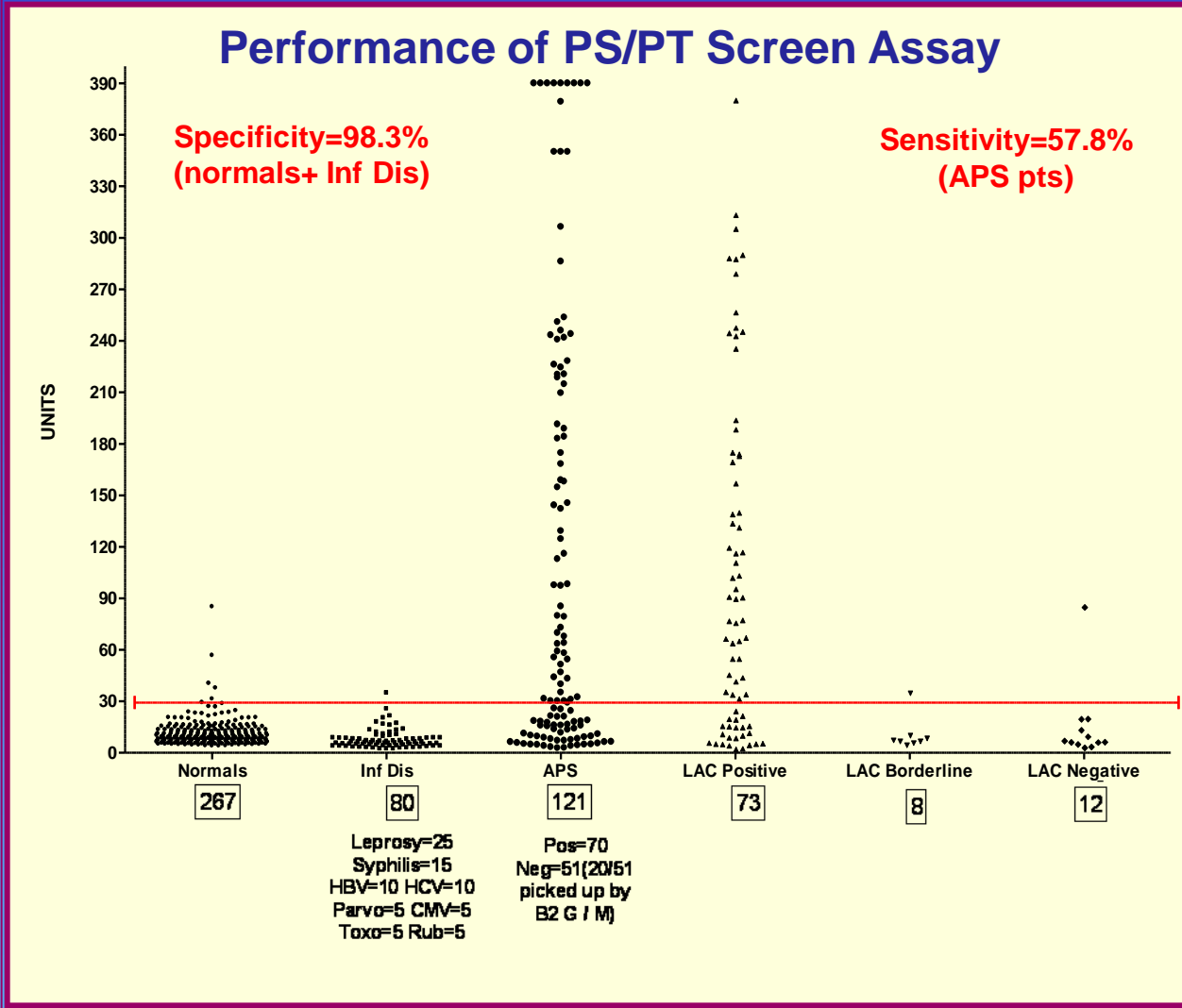
Abstract

Objective: To evaluate the performance and clinical utility of a prototype anti-phosphatidylserine/prothrombin (PS/PT) screening ELISA designed to detect both IgG and IgM antibodies to PS/PT complex in human serum or plasma.

Method: Sera from 121 patients with clinical diagnosis of APS, 267 random healthy controls, 80 from the infectious disease group and 93 sera known to be Lupus Anticoagulant (LAC) positive were tested on the new anti-PS/PT IgG/IgM ELISA assay (INOVA Diagnostics, San Diego, CA). Sera were also tested on individual PS/PT IgG and PS/PT IgM ELISA, Beta 2 GPI IgG and Beta 2 GPI IgM, ACA III IgG and ACA III IgM (INOVA Diagnostics, San Diego, CA). Sera from the APS and Infectious disease group were also evaluated with anti-PS IgG and anti-PS IgM ELISA kits. (The Binding Site).

Results: 70 of the 121 clinically diagnosed APS patients were positive for PS/PT screen giving a sensitivity of 57.8%. From the 267 random normals 5 were positive on the PS/PT screen and 1 (CMV+) from the infectious disease group conferring a specificity of 98.3%. In the LAC group the PS/PT Screen picked up 50 /73 LAC positive samples, 1/8 borderline and 1/11 LAC negative specimens.

Conclusion: By the combined detection of both IgG and IgM PS/PT antibodies, the prototype PS/PT screening assay agreed with LAC test results in over 75% of the sera tested. It detected approximately 60% of the APS sera tested with very high specificity (98.3%). Testing with β_2 GPI and ACA assays complemented the PS/PT Screen by detecting additional patients some of which were only positive for 1 of the three assays. The PS/PT assay may prove to be a valuable tool for the screening of patients with suspected anti-phospholipid syndrome and it may be useful in screening for LAC positives.



		LAC Reference		
		Positive	Negative	Total
PS/PT Screen	Positive	51	1	52
	Negative	22	19	41
	Total	73	20	93

Agreement LAC and PS/PT Screen Assays on Sera Panel (clinical Hx unknown)

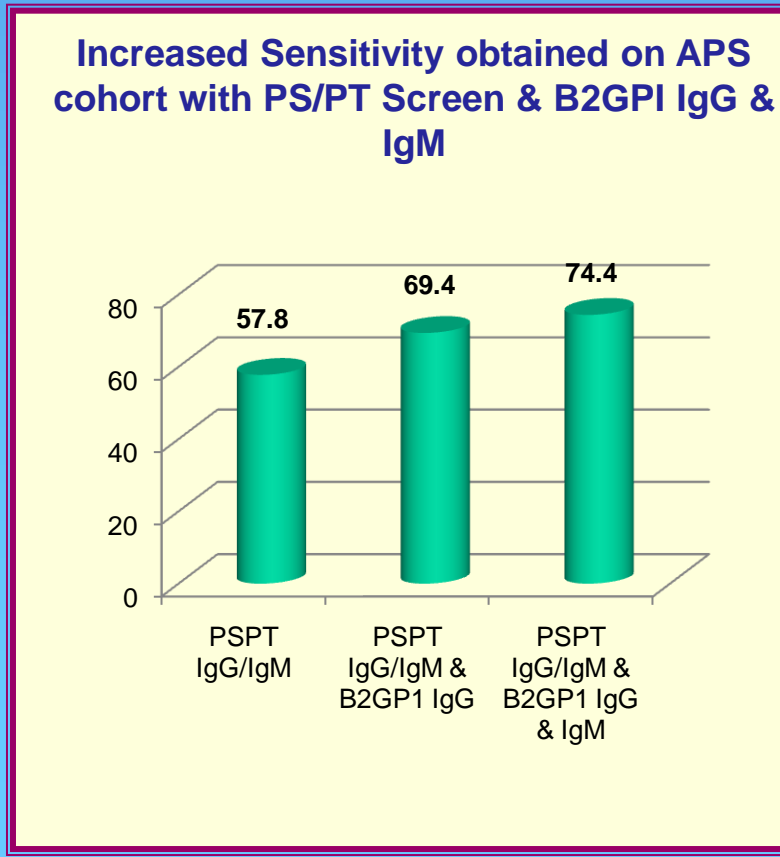
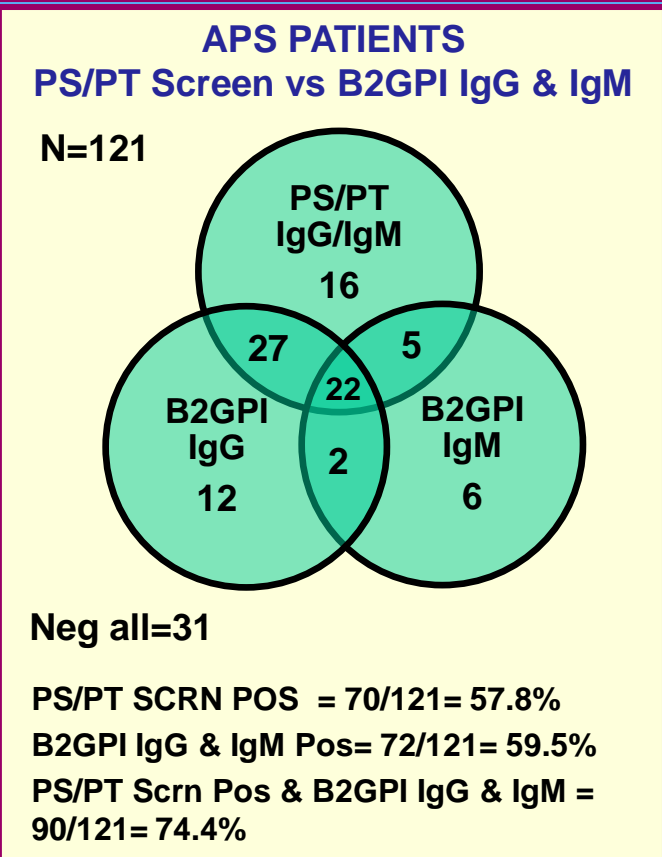
Overall Percent Agreement: 75.2%
Positive Percent Agreement: 68.9%
Negative Percent Agreement: 45.2%

Anti-phospholipid Assays on Infectious Disease Sera

DX	N	PS/PT	PS/PT	PS/PT	β_2	β_2	ACA	ACA	TBS PS	TBS PS
		Scr	IgG	IgM	IgG	IgM	IgG	IgM	G	M
Leprosy	25	0	0	2	0	11	4	7	5	9
Syphilis	15	0	0	0	1	1	3	1	1	0
HBV	10	0	0	0	0	0	0	0	1	0
HCV	10	0	0	0	1	1	3	0	2	0
Rubella	5	0	0	0	1	1	0	0	0	0
Parvo	5	0	0	0	0	0	0	0	0	2
CMV	5	1	1	0	0	0	1	0	1	0
Toxoplasma	5	0	1	0	0	0	0	0	0	0
Total	80	1	2	2	3	14	11	8	10	11

Background

Antiphospholipid antibodies (aPL) represent a large, heterogeneous group of immunoglobulins of considerable clinical importance due to their association with arterial and/or venous thrombosis, recurrent pregnancy loss, neurological disorders, pulmonary hypertension and thrombocytopenia. Detection of antibodies to anticardiolipin and the lupus anticoagulant (LAC) clotting assay have been the routine assays performed in clinical laboratories to aid in diagnosis of antiphospholipid syndrome (APS). Realization that the actual target of many aPL antibodies was the phospholipid binding protein β_2 GPI which bound to the cardiolipin antigen immobilized on the ELISA well, led to assays to specifically detect antibodies to β_2 GPI. Prothrombin (factor II) is another phospholipid binding protein with procoagulant activity. Several groups have clearly shown antibodies targeting the complex of phosphatidylserine (PS) and prothrombin (PT) have significant clinical relevance due to their strong correlations with clinical features of APS and with the presence of LAC (1-4). It was also shown that it is antibody to the PS/PT complex, rather than antibodies that target prothrombin alone, that correlate with LAC and APS. (3,4) The PS/PT antibodies provide useful sensitivity for APS and have high specificity. Their inclusion into the laboratory criteria for classification of APS has been proposed (4). We have demonstrated that detection of PS/PT IgG and IgM antibodies identifies a majority of LAC and APS positive patients. We now show that a combined IgG/IgM PS/PT screening assay can approximate the results obtained with the individual assays.



CONCLUSIONS

- The new PS/PT Screen detects both IgG and IgM antibodies to the phosphatidylserine/prothrombin complex with high specificity.
- The assay can be run with serum or citrated plasma (data not shown).
- The PS/PT Screen detects a majority of APS patients including many that are β_2 GPI negative.
- β_2 GPI IgG & IgM testing can complement the PS/PT Screen assay for identification of additional APS patients.
- The prototype PS/PT Screen agreed with LAC test results in over 75% of the sera tested and may prove to be a useful alternative to the complex LAC assay for screening suspected APS patients.

REFERENCES

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