Objective: C4BP is a complement inhibitor with anticoagulant function. Its main isoform is bound to protein S in the circulation. Levels of both protein S and C4BP are known to be reduced by warfarin treatment (2) as well as by aPL, a main antigen in APS. Therefore we compared the levels of C4BP in different subgroups (67 pAPS, 118 SLEaPL+, 291 SLEaPL-, 322 controls) to investigate the levels of C4BP in primary (p) and secondary (s) APS, also considering warfarin treatment.

Methods: The total amount of C4BP (C4BPt) was measured by using magnetic carboxylated microspheres which were coupled with a monoclonal antibody against the α-chain of human-C4BP to capture the antigen. To detect C4BP the same antibody was used, biotinylated. The binding of biotinylated antibodies was detected by streptavidin-phycoerythrin and data were collected using a MAGPIX Multiplex Reader. Using independent t-test, we compared C4BP in 118 SLE patients with repeated positivity for Antiphospholipid antibodies (aPL) (39/118 on warfarin), 291 aPL negative SLE patients (16/291 on warfarin), 67 pAPS (33/67 on warfarin), and 322 controls (none on warfarin). We then performed an interaction and a mediation analysis (3) in the SLE group to study the impact of warfarin on C4BP levels: since warfarin is mostly prescribed to aPL+ patients, it is considered a mediator in the reducing effect of aPL on C4BP. Therefore we compared individuals exposed and non-exposed to the presence of aPL with or without the mediator warfarin and calculated the percentage of reduction in C4BP that could be attributed to aPL or warfarin.

Results: Overall C4BP is 20% reduced in aPL+ patients (fig 1), independently of SLE, past thrombotic events and nephritis. Warfarin treated patients have lower levels of C4BP (fig 2). According to mediation analysis 11% of C4BP reduction is due to aPL and 9% to warfarin.

Conclusion: Both aPL and warfarin decrease levels of C4BP, a complement and coagulation regulator. Reduction of this complement inhibitor could contribute to complement activation and thrombosis in APS. Our results raise new questions regarding the effects of warfarin treatment on complement and coagulation in APS.