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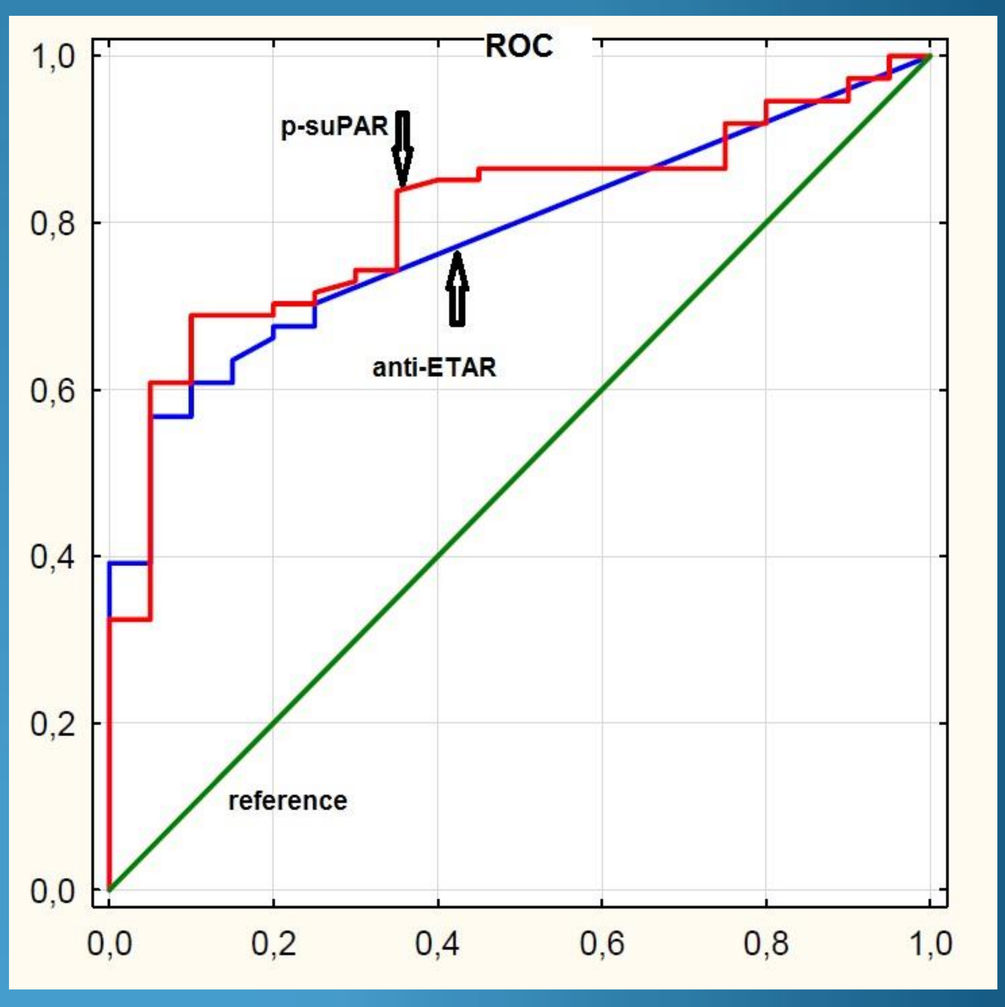
# ANTI-ETAR AND SUPAR AS SURROGATE MARKERS OF DISEASE ACTIVITY IN RENAL ANCA-ASSOCIATED VASCULITIS

**INTRODUCTION AND AIMS:** ANCA-associated vasculitides (AAV) are a group of multisystem autoimmune disorders affecting small-sized vessels. At present, there is a lack of reliable markers of disease activity in AAV, hence the need for reliable biomarkers of disease activity. Thus we hypothesized that serum anti-endothelin-1 type A receptor (anti-ETAR) antibodies and plasma soluble urokinase plasminogen activator receptor (suPAR) as candidate biomarkers might be able to distinguish between active disease and remission in renal AAV.

**METHODS:** Sixty patients (mean age 59.3 ± 13 yrs) with renal AAV were enrolled in this prospective observational study (34 M, 26 F); 31 were PR3-ANCA positive, 27 were MPO-ANCA positive while 2 were ANCA negative. Exclusion criteria: procalcitonin level >0,2 ng/ml, recent antibiotic course, recent cardiovascular event or surgery (4 weeks). Anti-ETAR antibodies and suPAR were assayed by ELISA. Disease activity was assessed using Birmingham Vasculitis Activity Score (BVAS). Patients were divided into 2 subgroups based on disease activity namely: active disease subgroup (BVAS≥1) and remission subgroup (BVAS=0). Area under the ROC curve (AUC) for serum anti-ETAR and plasma suPAR (p-suPAR) were used for calculation of sensitivity and specificity in AAV.

**RESULTS:** AAV patients with active disease had a higher level of serum/plasma anti-ETAR and sUPAR in comparison with those patients in remission (table 1). Anti-ETAR antibodies in any level were found in 26 pts (43%); in 21 with active AAV (BVAS≥1). Setting a derived optimum cutoff for p-suPAR of 4,94 ng/ml (from Youden's index) for detection of active renal AAV resulted in a sensitivity of 69% and a specificity of 90% and a positive likelihood ratio (LR) of 6.9. Area under the ROC curve (AUC) for p-SUPAR was 0.807 (Fig.1) Cutoff for serum anti-ETAR of 3,35 U/ml resulted in a sensitivity of 57% , specificity of 95% and a positive LR of 11.4. AUC for serum anti-ETAR was 0.783.

| Table 1. (Mann_Whitney U test) | BVAS=0 (mean) | BVAS >=1 (mean) | P value |
|---|---|---|---|
| AAV duration (m) | 59 | 50.5 | 0.56 |
| P-suPAR ng/ml | 3.6 | 8.0 | 0.008 |
| BVAS | 0.00 | 7.40 | 0.000 |
| VDI | 2.80 | 3.38 | 0.43 |
| Anti-ETAR U/ml | 0.78 | 5.39 | 0.0226 |




**CONCLUSIONS:** Our study indicated that serum anti-ETAR and plasma suPAR levels were elevated in patients with active renal AAV. AUC calculations showed better performance for plasma suPAR than anti-ETAR as a surrogate marker of AAV activity. Plasma suPAR above 4,94 ng/ml served as a marker for disease activity with a sensitivity of 69% and a specificity of 90% .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