Improving Hypertension Control by Molecular Stratification of First-Line Non-Responders using RAAS Triple-A Testing

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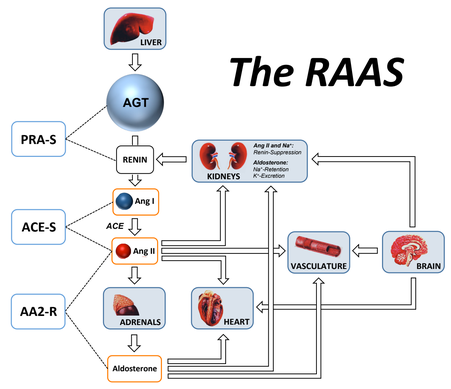
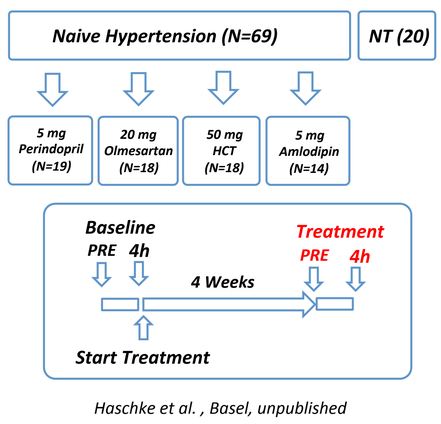
Background

RAAS **Triple-A** testing is based on a clinical high-throughput mass-spectrometry assay for simultaneous quantification of **A**ngiotensin I, **A**ngiotenin II and **A**ldosterone in standard serum by RAAS equilibrium analysis. Equilibrium angiotensin and aldosterone levels are used to calculate markers for renin-activity (PRA-S), angiotensin-converting-enzyme activity (ACE-S) and adrenal function (AA2-Ratio). The response of these markers to different drugs was investigated in hypertensive patients on single drug therapy. The diagnostic performance of the AA2-Ratio in screening for primary aldosteronism (PA) has been compared to the aldosterone-to-renin ratio (ARR) as putative gold standard in 110 resistant hypertensive patients, revealing advantages of the AA2-Ratio especially in terms of drug interference. ACE-S was shown to be highly predictive for ACEi intake within previous 24h. Combining the results from several validation studies, a PRA-S, ACE-S and AA2-Ratio based stratification scheme for hypertensive patients has been developed. The algorithm can identify patients with primary aldosteronism and is able to detect compliance or dosing issues for ACE inhibitors and ARBs.

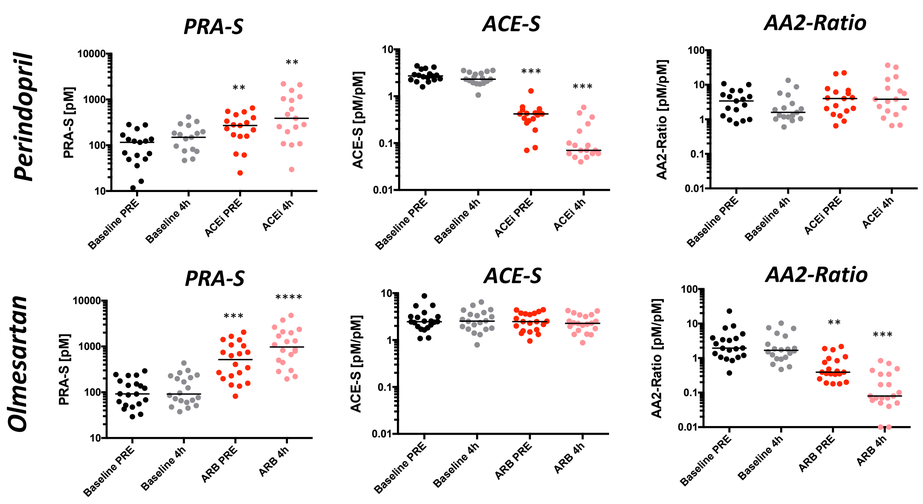


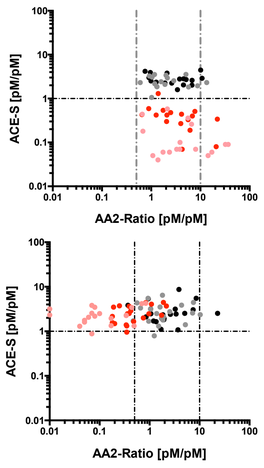
Renin-Angiotensin-Aldosterone-System

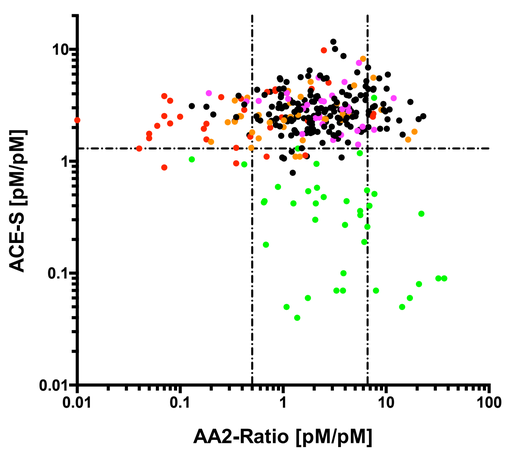
RAAS Triple-A Parameters in Hypertension – Drug Effects



Haschke et al. , Basel, unpublished



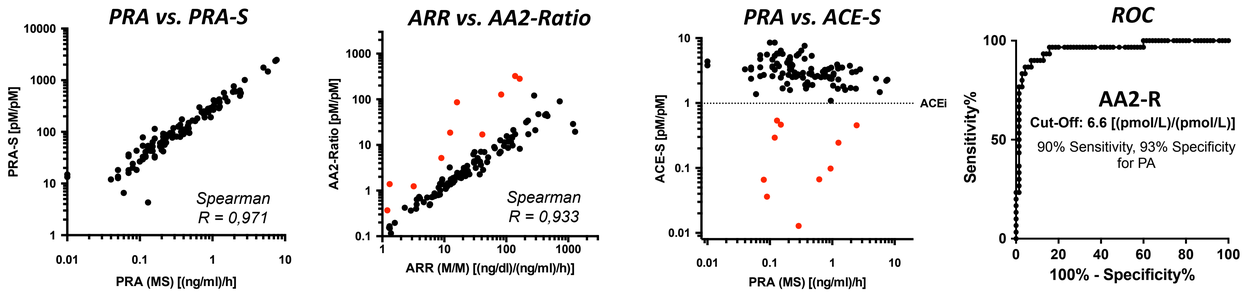




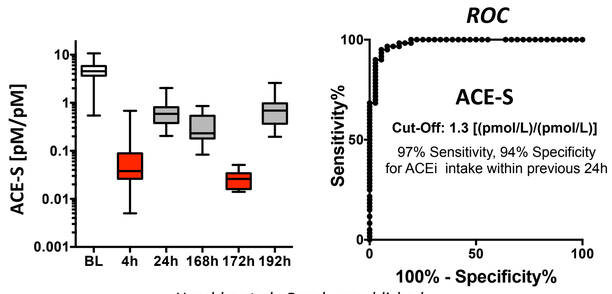
The AA2-Ratio: A Novel Screening Test for Primary Aldosteronism (PA)

110 Patients
(77 EH + 33 PA)

Mulatero et al., Hypertension 2019



ACE-S: Functional Drug Monitoring

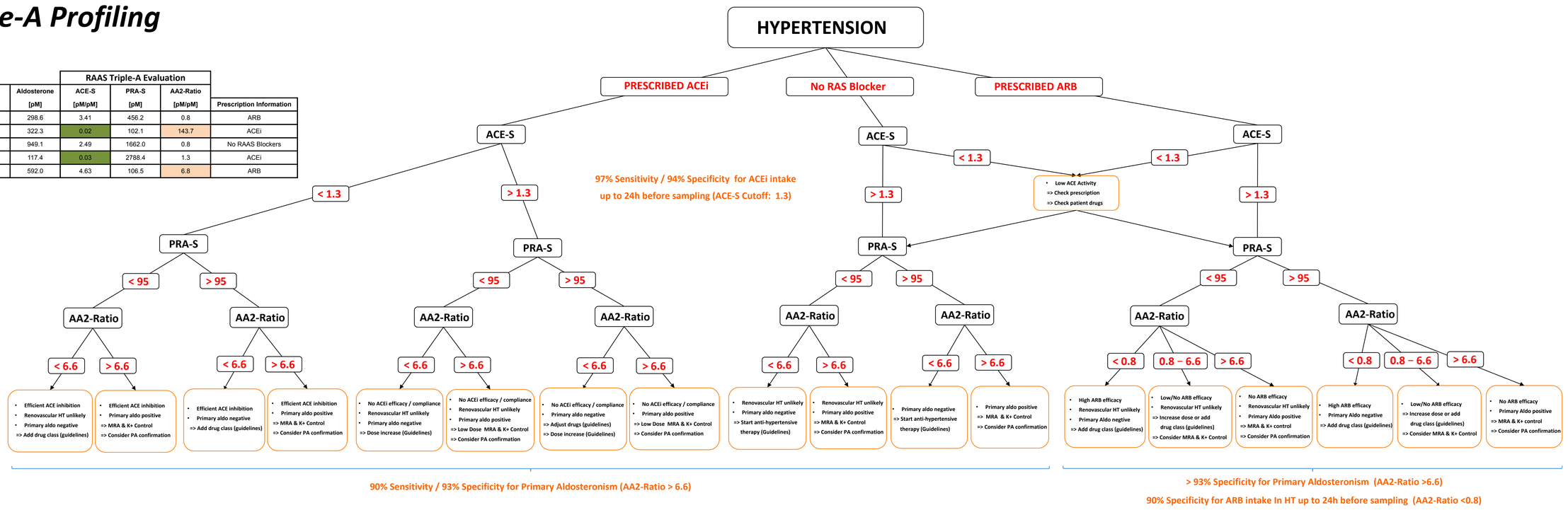


Haschke et al., Basel, unpublished

RAAS Triple-A Profiling

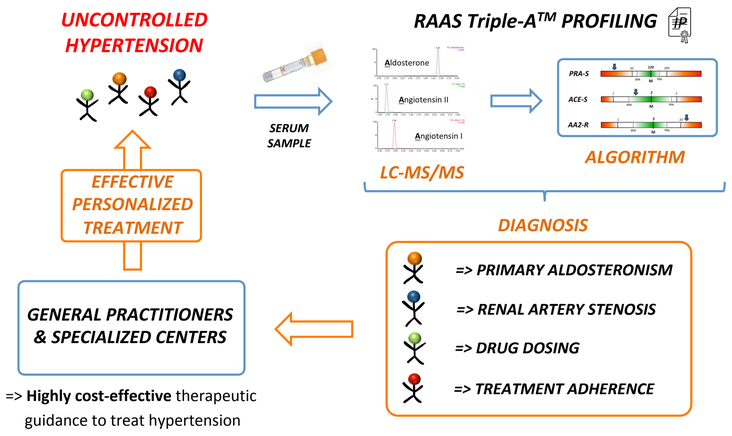
GP-Patient Examples:

	RAAS Triple-A Evaluation						
	Ang II [pM]	Ang I [pM]	Aldosterone [pM]	ACE-S [pM/pM]	PRA-S [pM]	AA2-Ratio [pM/pM]	Prescription Information
Patient 1	352.6	103.6	298.6	3.41	456.2	0.8	ARB
Patient 2	2.2	99.9	322.3	0.02	102.1	143.7	ACEi
Patient 3	1130.5	449.8	949.1	2.49	1662.0	0.8	No RAAS Blockers
Patient 4	91.0	2697.4	117.4	0.03	2788.4	1.3	ACEi
Patient 5	87.6	18.9	592.0	4.63	106.5	6.8	ARB



Conclusions

RAAS Triple-A analysis for the first time provides insights into a patient's RAAS at the level of multiple effector hormones simultaneously. The system's patient specific biochemical constitution and pharmacologic response to anti-hypertensive therapies is characterized by a single high-throughput test. Combining this novel opportunity with clinical information, a stratification scheme could be developed that identifies potential secondary causes of hypertension as well as dosing issues and drug adherence problems as underlying causes for uncontrolled hypertension. RAAS Triple-A based diagnostic profiling of uncontrolled hypertension has the potential to trigger significant changes in hypertension care by introducing personalized treatments based on an easily available and usable diagnostic tool not only for specialized centers but also for general practitioners. Further studies are required to assess the performance and health economic impact of the suggested process in large and inhomogeneous patient cohorts.



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