

Plasma angiotensin profiling in hypertensive patients screened for primary aldosteronism

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Objective:

- The plasma aldosterone-to-renin ratio (ARR) is the recommended laboratory parameter to screen for primary aldosteronism (PA). However, renin measurements are unreliable at very low concentrations. Instead, plasma angiotensin (Ang) I and its metabolites may be quantitated by mass spectrometry.
- We investigated, if Ang fragments and Aldo/Ang correlate with, and can replace, ARR in clinical routine.

Prospective observational study, n=24

- Academic hypertension clinic; new referrals screened over 12 months
- Inclusion** : uncontrolled hypertension despite ≥ 2 antihypertensives
- Exclusion**: major comorbidity, renal failure $>2^\circ$, mandatory RAAS blockers
- Mean age 54 ± 13 years, 42% female
- ARB 50%, ACE-Inhib. 29%, diuretics 67%, β -blocker 54%

Clinical study protocol

Pre-screening visit: drugs incompatible with A/R tests are stopped (ACEI, ARB, diuretics, β -blocker, central), calcium or α -blockers allowed,
Screening visit: aldosterone/renin ratio (ARR) supine + upright, Ang supine, standardized blood sampling 8:30-9:30 am; ≈ 14 days later

Mass spectrometric quantification of 10 Ang (LC-MS/MS):

(Ang I [1-10], Ang II [1-8], Ang 1-7, Ang 1-9, Ang III (2-8), Ang 3-7, Ang 1-5, Ang IV (3-8), Ang 2-7, Ang 2-10); all supine, on screening visit

- Native plasma concentrations
- After in-vitro plasma auto-incubation (equilibrium concentrations, renin-dependent)

Aldosterone: mass spectrometry; renin: immunoassay (Cisbio®)
Preliminary analysis

Plasma parameters

	Pre-screening visit	Screening visit
Ang I (pmol/l)	35 \pm 73	2.5 \pm 2.6
Ang II (pmol/l)	22 \pm 54	2.6 \pm 2.4
Ang I, eq. (pmol/l)	293 \pm 489	41 \pm 57 [19]
Ang II, eq. (pmol/l)	419 \pm 1000	96 \pm 119 [44]
Ang I + Ang II eq. (pmol/l)	712 \pm 1398	115 \pm 146
Renin, supine (ng/l)	-	9.1 \pm 11.8 [5.1]
Renin, upright (ng/l)	-	13.3 \pm 13.8 [8.2]**
Aldosterone, supine (pmol/l)	-	146 \pm 120 [122]
Aldosterone, upright (pmol/l)	-	324 \pm 205 [305]**
ARR, supine (pmol/ng)	-	32 \pm 34
ARR, upright (pmol/ng)	-	39 \pm 34 ^b
Ald/Ang I eq, supine (pmol/pmol)	-	7.7 \pm 9.7
Ald/Ang II eq, supine (pmol/pmol)	-	3.8 \pm 5.5

Ald, aldosterone; ARR, ald/renin ratio; eq., equilibrium

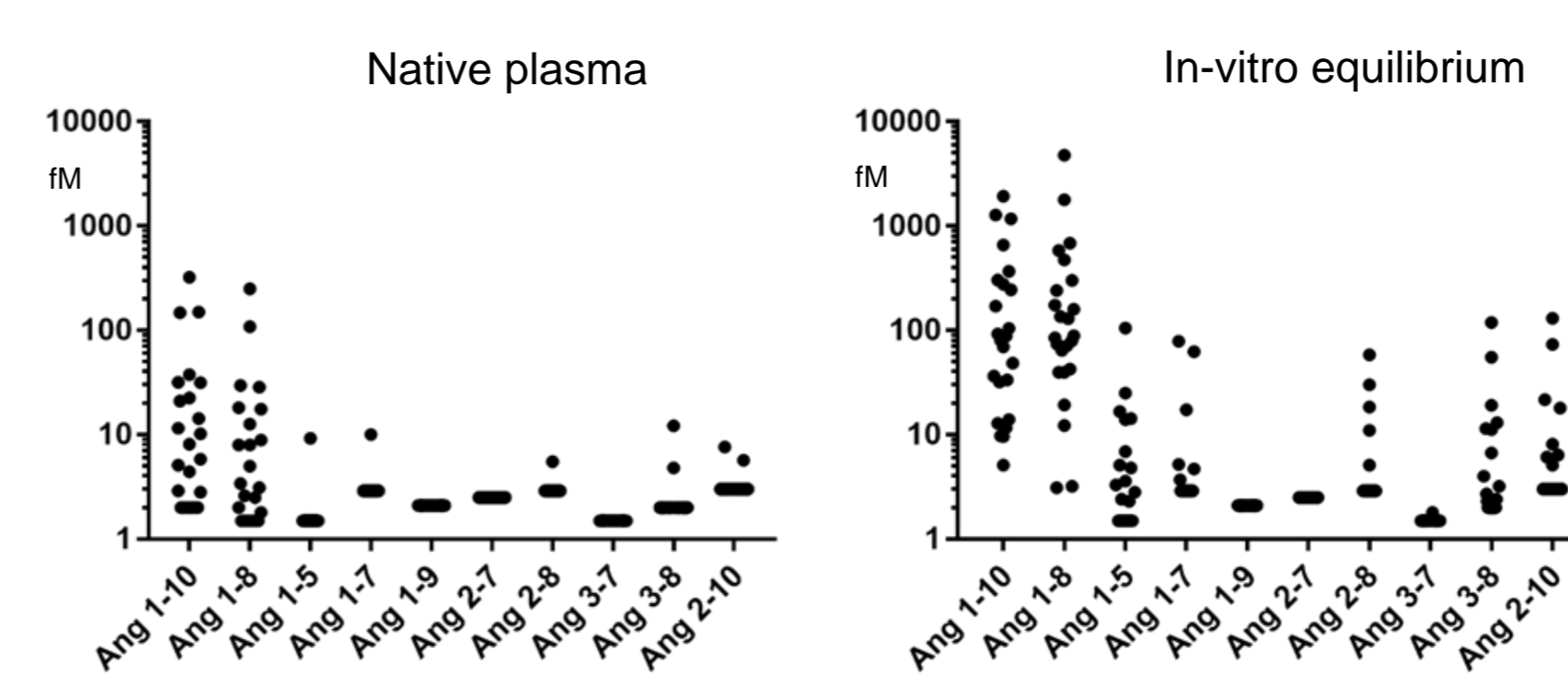
Correlation coeff. r (Pearson)

	Ang II eq. sup.	Ang I eq. sup.	Aldosterone supine	Aldosterone upright	Renin supine	Renin upright
Ang II, eq. supine	1	0.93**	<0.2	<0.2	0.94**	0.95**
Ang I, eq. supine		1.00	<0.2	<0.2	0.97**	0.95**
Aldosterone, supine			1.00	0.73**	<0.2	<0.2
Aldosterone, upright				1.00	<0.2	<0.2
Renin, supine					1.00	0.96**
Renin, upright						1.00

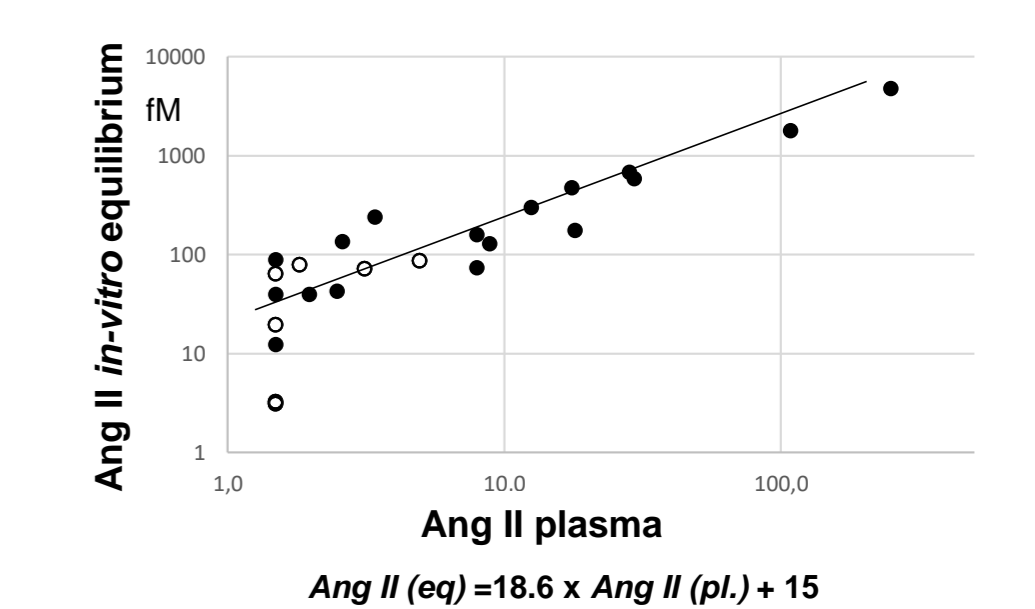
** p<0.01; no significant correlation of urinary aldosterone excretion with Ang II, Ang I or Ald/Ang (p=NS)

Angiotensins in plasma and after in-vitro incubation (equilibrium)

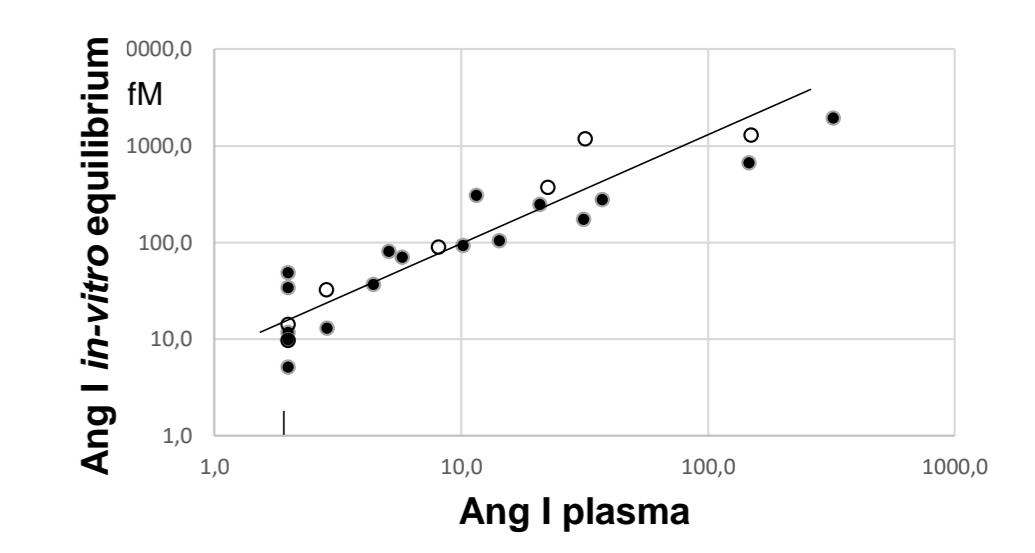
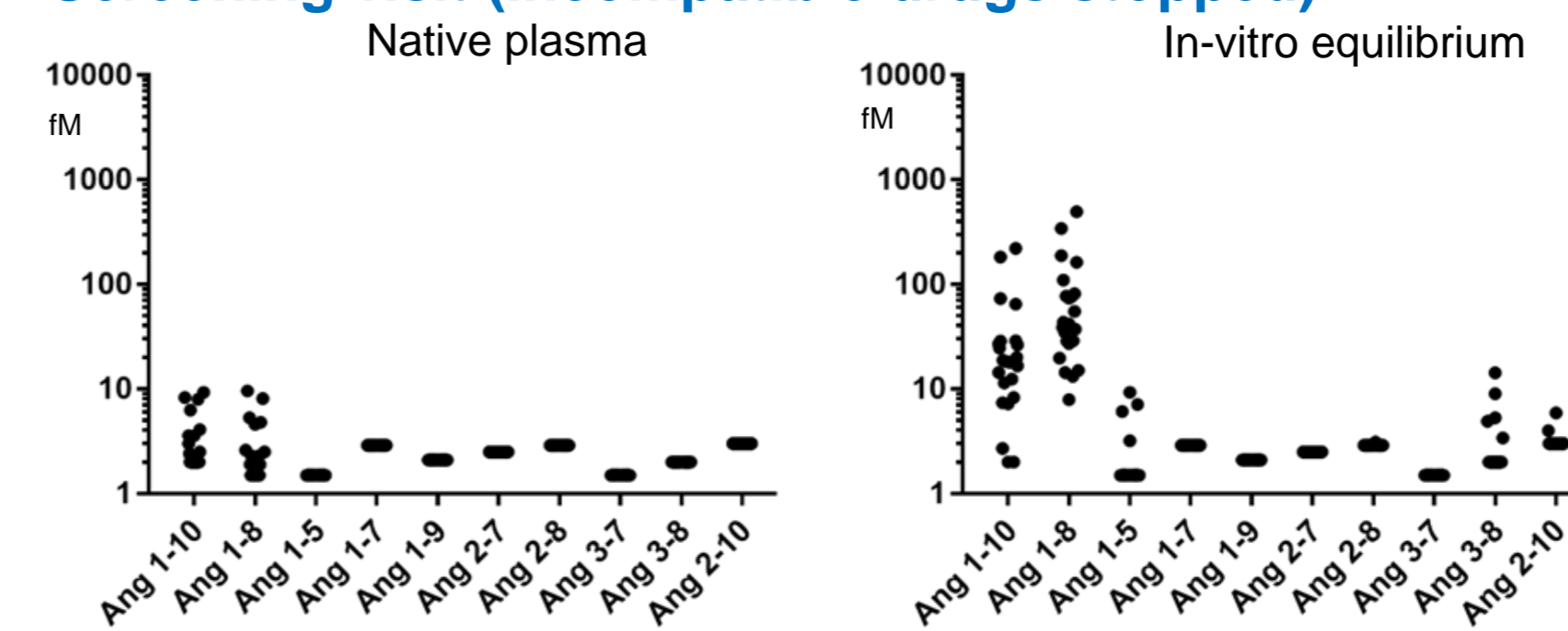
Pre-screening visit (under antihypertensive treatment)



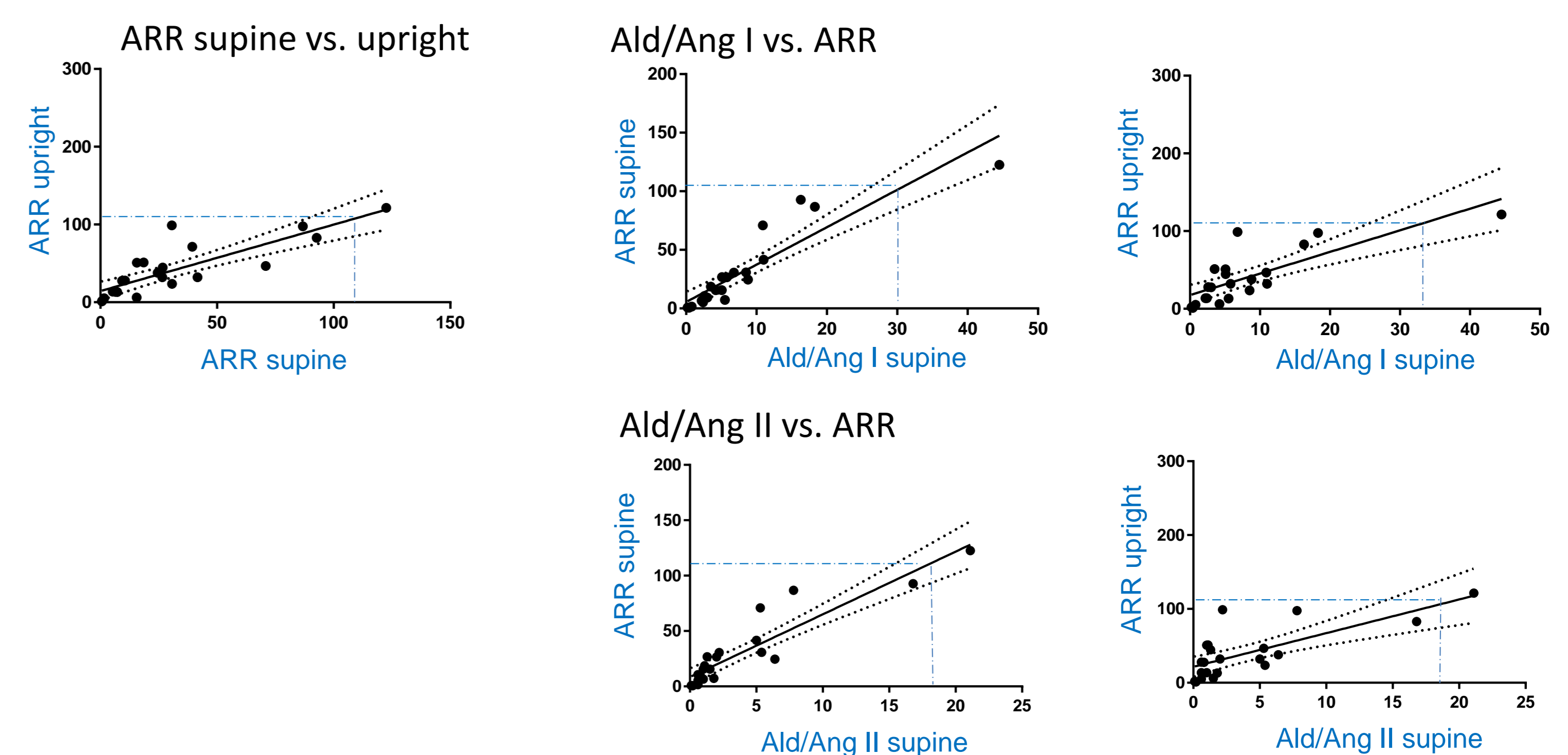
Prescreening visit



Screening visit (incompatible drugs stopped)



Screening visit (incompatible drugs stopped), eq. Ang



ARR cut-off for PA = 105 (guidelines)
Ald/Ang I cut-off for PA ~ 30
Ald/Ang II cut-off for PA ~ 20

Correlation coeff. r ^a	ARR supine	Ald/Ang I, supine	Ald/Ang II, supine	ARR upright
ARR, supine	1.00	0.91**	0.92**	0.84**
Ald/Ang I, supine		1.00	0.92**	0.78**
Ald/Ang II, supine			1.00	0.73**

** p<0.01; Ald, aldosterone; ARR, ald/renin ratio; ^a all equilibrium Ang concentrations after autoincubation of plasma; Pearson's r

Conclusions:

- Ald/Ang I or Ald/Ang II based on incubated plasma may safely replace ARR during screening for primary aldosteronism**
- Ald/Ang may be more accurate than ARR at low renin concentrations**

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