COMPARISON BETWEEN ALDOSTERONE AND RENIN MEASUREMENT BY CHEMILUMINESCENT IMMUNOASSAY AND RADIOIMMUNOASSAY FOR THE DIAGNOSIS OF PRIMARY ALDOSTERONISM

Burrello J, Buffolo F, Monticone S, Viola A, Williams TA, Lucchiari M, Mengozzi G, Rabbia F, Veglio F, Mulatero P - Division of Internal Medicine and Hypertension Unit, Department of Internal Medicine, University of Torino, Torino, Italy

BACKGROUND

Primary aldosteronism (PA) is the most frequent cause of secondary hypertension responsible for an increased rate of cardiovascular events. According to the Endocrine Society Guidelines, up to 50% of hypertensive patients should be screened for PA, using the aldosterone to renin (or plasma renin activity, PRA) ratio (AARR and ARR, respectively). The automated Diasorin LIAISON® chemiluminescent immunoassay for renin and aldosterone measurement became available and in many laboratories is currently used instead of the classical radioimmunometric PRA and aldosterone assay.

OBJECTIVE

Aim of the study was to prospectively compare the diagnostic accuracy of AARR and ARR as screening test for PA and the two aldosterone assays also during confirmatory test in patients with a positive screening test.

DESIGN & METHODS

Clinical characteristics and hormonal parameters of the patients are summarized in Table 1. One hundred patients were screened for PA and 44 patients underwent confirmatory test (either by intravenous saline load or by captopril challenge test). We considered as cut off for the AARR 2.7 (ng/dL/mU/L) and for the ARR 30 (ng/dL/ng/mL/h). All patients positive to one of the two screening tests underwent confirmatory test; patients with positive confirmatory test underwent subtype diagnosis by CT scanning and adrenal vein sampling. For the design of the study see **Figure 1**.

	Totale	EH	PA	P-value EH vs PA	BAH	APA	Overall P-value	P-value EH vs APA	P-value EH vs BAH	P-value APA vs BAH
Number of patients	100	73	27	-	22	5	-	-	-	-
Age (years)	49,36	47,56	54,22	_0,006_	53,55	57,2	0,019	0,157	0,068	1
Sex (%) (Male/Female)	54 / 46	54,8 / 45,2	51,9 / 48,1	0,793	45,5 / 54,5	80 / 20	0,363	0,272	0,592	0,163
SBP (mmHg)	146,65	145,41	150,00	0,236	144,77	173,00	_0,001_	_0,001_	1	_0,002_
DBP (mmHg)	91,35	91,85	90,00	0,672	88,64	96,00	0,238	1	0,562	0,416
K+ (mEq/L)	4,071	4,230	3,633	_<0,001_	3,750	3,120	_<0,001_	_<0,001_	_<0,001_	0,027
PRA in RIA (ng/mL/h)	25° 0,1525 50° 0,5500 75° 1,7100	25° 0,3300 50° 1,0100 75° 2,0450	25° 0,1000 50° 0,1300 75° 0,3000	_<0,001_	25° 0,1000 50° 0,1400 75° 0,3175	25° 0,1000 50° 0,1000 75° 0,1400	_<0,001_	_0,003_	_<0,001_	1
DRC in CL (mU/L)	25° 4,2655 50° 14,2950 75° 28,1950	25° 10,3000 50° 20,3300 75° 35,8100	25° 2,8520 50° 3,5770 75° 8,6310	_<0,001_	25° 2,8760 50° 3,9640 75° 9,0475	25° 2,2325 50° 3,0530 75° 3,6210	_<0,001_	_0,001_	_<0,001_	0,745
AC in RIA (ng/dL)	25° 12,03 50° 17,10 75° 26,08	25° 8,90 50° 14,70 75° 22,90	25° 18,00 50° 23,20 75° 28,40	_<0,001_	25° 17,78 50° 23,55 75° 28,03	25° 19,00 50° 20,00 75° 30,90	_<0,001_	0,119	_0,001_	1
AC in CL (ng/dL)	25° 9,715 50° 13,500 75° 19,075	25° 9,030 50° 11,900 75° 17,000	25° 16,200 50° 19,200 75° 22,500	_<0,001_	25° 15,650 50° 18,250 75° 21,675	25° 20,150 50° 22,800 75° 39,200	_<0,001_	_0,003_	_0,001_	0,579
Pharmacological Wash-out (%)	23	24,7	18,5	-	22,7	20	-	-	-	-

Table 1. **Characteristics of the population screened** - *EH, essential hypertension; PA, primary aldosteronism; BAH, bilateral adrenal hyperplasia; APA, aldosterone-producing adenoma; SBP, systolic blood pressure; DBP, diastolic blood pressure; K+, potassium; PRA, plasma renin activity; DRC, direct renin concentration; AC, aldosterone concentration.*
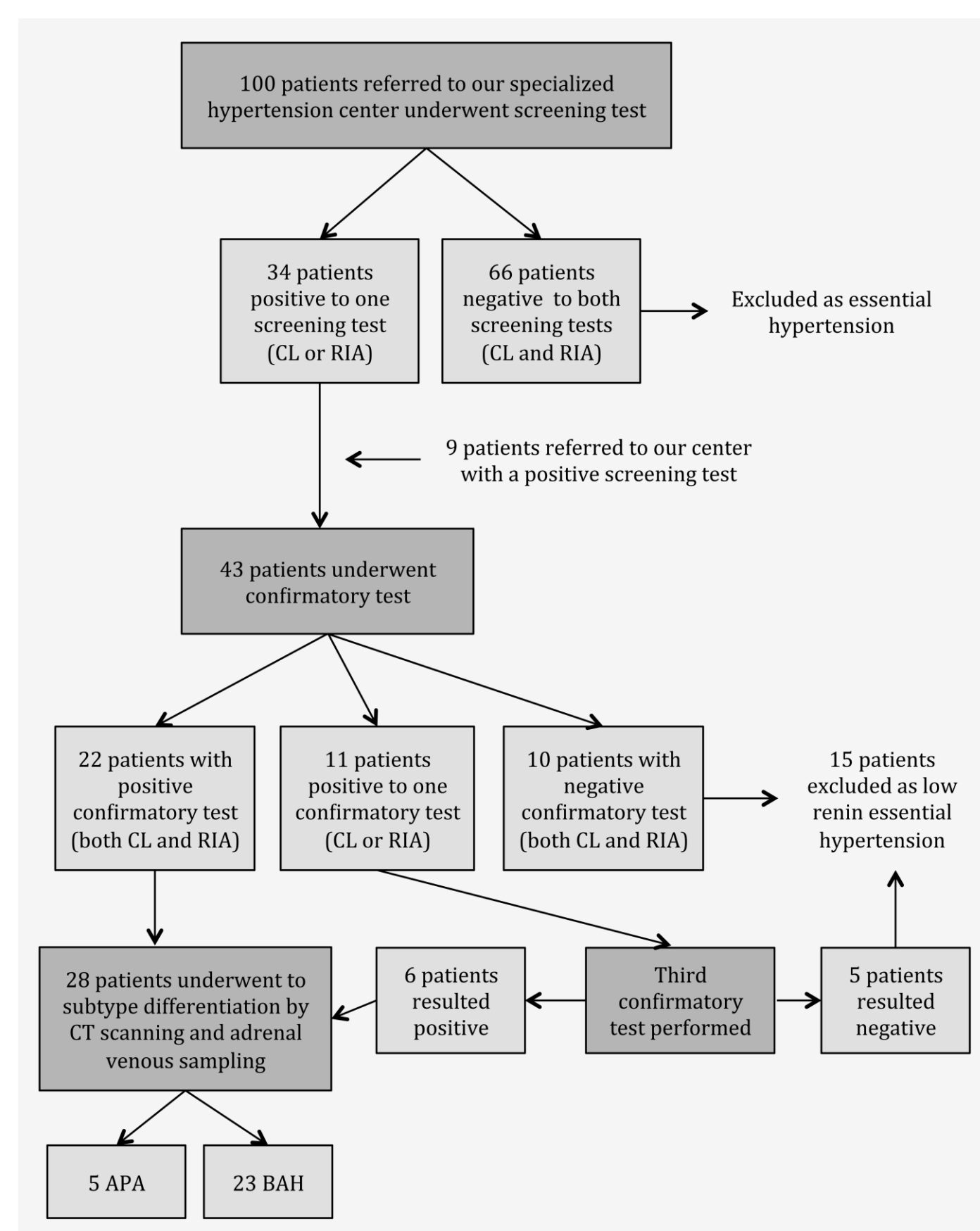
RESULTS

Figure 1. **Patients Selection** - *EH, essential hypertension; BAH, bilateral adrenal hyperplasia; APA, aldosterone-producing adenoma; CL, chemiluminescence; RIA, radioimmunoassay. We screened for PA 100 patients referred to our center; 66 resulted negative to both screening tests (CL and RIA) and were excluded as essential hypertensives; 34 patients resulted positive to one screening test (CL or RIA) and underwent confirmatory test together with 9 patients referred to our center with a positive screening test performed elsewhere. We performed 43 confirmatory test (32 intravenous saline load and 11 captopril challenge test); 22 resulted positive (both CL and RIA) and underwent subtype differentiation, whereas 10 negative (excluded as low renin essential hypertension); 11 patients underwent a third confirmatory test for discrepancy between the two tests: 6 resulted positive and underwent subtype differentiation and 5 resulted negative and were excluded as low renin essential hypertension. In the overall population of 109 patients we diagnosed 5 APA (4,6%), 23 BAH (21,1%) and 81 EH (74,3%).*

Seventy three patients were diagnosed as essential hypertensives, 22 had bilateral adrenal hyperplasia and 5 had an aldosterone producing adenoma (APA). The AARR displayed a sensitivity of 78% and a specificity of 100%, whereas the ARR had a sensitivity of 96% and a specificity of 90%. Of the 6/27 PA patients missed by AARR, none resulted to be affected by APA. All PA patients were correctly diagnosed by chemiluminescence at confirmatory test. In the overall sample of 181 measurements available both the correlation for the PRA with renin (**Figure 2a and 2b**) and for aldosterone (**Figure 3a**) in chemiluminescence and radioimmunoassay were highly significant (Rho=0.66, p<0.0001 and Rho=0.80, p<0.0001, respectively). Bland-Altman plot comparing the AC measurement in RIA vs CL is displayed in **Figure 3b**. On ROC curves (**Figure 4**), the AUC for AARR was 0.905 (95% CI 0.821-0.988) and for ARR 0.947 (95% CI 0.903-0.991) and they were not significantly different.
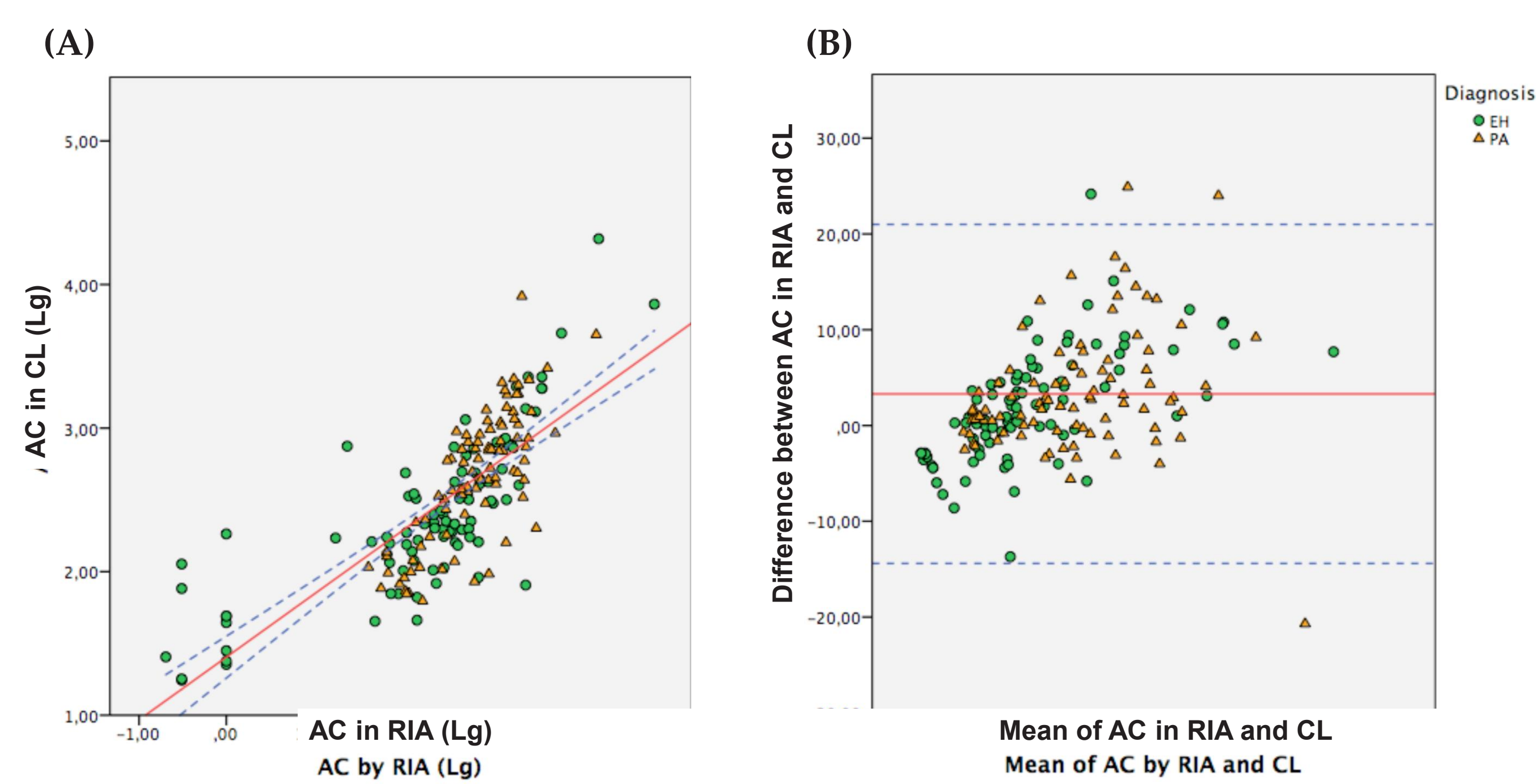

Figure 2. **Regression curve** *of DRC in CL versus PRA in RIA - PRA, plasma renin activity (expressed in ng/mL/h); DRC, direct renin concentration (expressed in mU/L); CL, chemiluminescence; RIA, radioimmunometric assay; Lg, natural logarithm; EH, essential hypertension; PA, primary aldosteronism. On X-assis PRA by RIA natural logarithm; on Y-assis DRC by CL natural logarithm; circles: EH; triangles: PA; dashed lines: confidence interval; continuous line: regression curve. (A) DRC by CL versus PRA by RIA: n = 181; R^2 = 0,502; Y = 2,84 + 0,71*X. (B) DRC by CL versus PRA by RIA for patients with PRA < 1 ng/mL/h or DRC < 12 mU/L: n = 142; R^2 = 0,121; Y = 2,38 + 0,44*X.*

Figure 3. **Regression curve and Bland-Altman plot of AC in CL versus RIA**– *AC, aldosterone concentration (expressed in ng/dL); CL, chemiluminescence; RIA, radio-immunometric assay; Lg, natural logarithm; EH, essential hypertension; PA, primary aldosteronism. Circles: EH; Triangles: PA. (A) AC by CL versus RIA: n = 181; R^2 = 0,593; Y = 1,4 + 0,44*X. Dashed lines: confidence interval; continuous line: regression curve. (B) Bland-Altman plot: comparison between AC by CL versus RIA. Continuous line indicates mean difference between AC measurement by CL and RIA; dashed lines indicate difference mean value ± 1,96 standard deviations (IC 95%).*
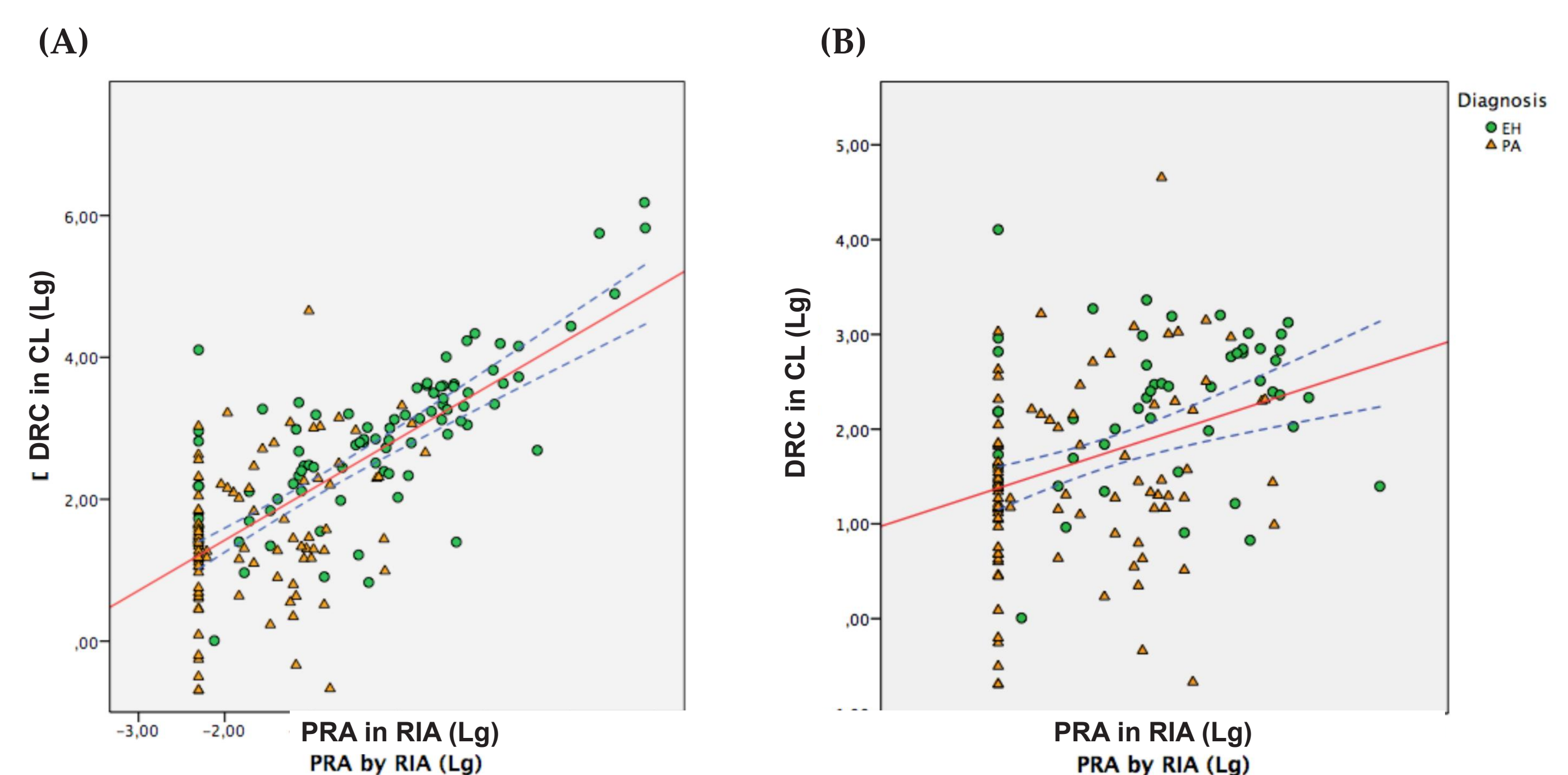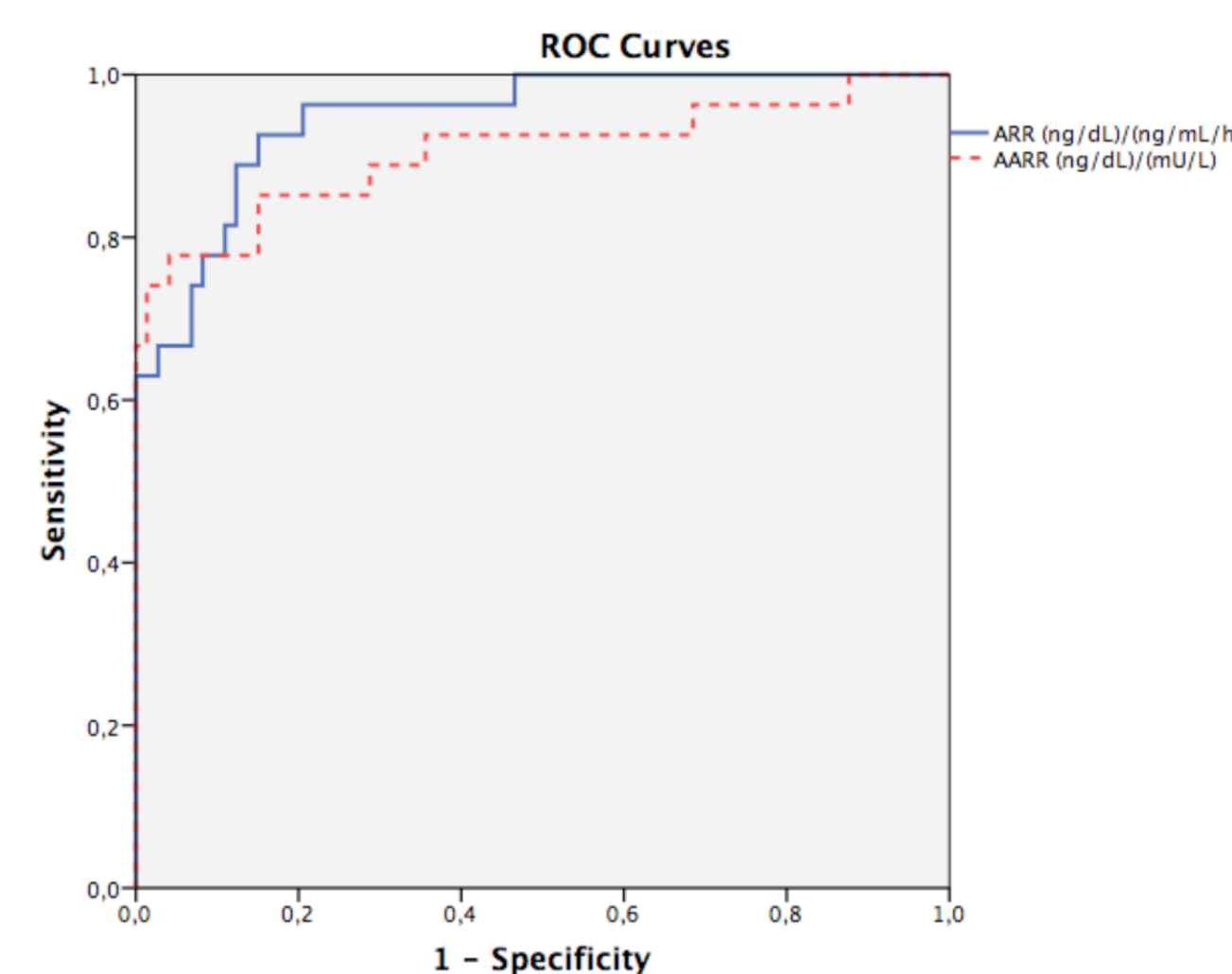

Figure 4. **ROC curves for AARR and ARR** - *On X-assis 1 - Specificity; on Y-assis Sensitivity. Dashed line: ROC curve for AARR; the AUC was 0,905 (95% CI 0,821-0,988). Continuous line: ROC curve for ARR. The AUC was 0.947 (95% CI 0,903-0,991). AUC values are not significantly different (P > 0,05).*

CONCLUSIONS

The AARR using aldosterone and renin mesured in CL with the DIASORIN LIAISON® automated method display similar diagnostic performance compared with the classical ARR using aldosterone and PRA measured with the RIA method. In particular none of the patients with aldosterone-producing adenomas were missed using the CL measurements both for the screening and the confimatory/exclusion tests. Therefore, the authomated aldosterone and renin chemiluminescent assay is a reliable alternative to the well-established radioimmunometric method in the diagnosis of primary aldosteronism.

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