Deterioration of indices of insulin resistance in patients with non-functioning and cortisol secreting adrenal incidentalomas during a long term follow-up

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OBJECTIVES

- Adrenal incidentalomas (AI) with or without concomitant autonomous cortisol secretion can be associated with several metabolic alterations that may lead to increased cardiovascular risk*. However, data regarding insulin resistance (IR) during long term follow-up of AI are scarce.
- The aim of the study was to prospectively investigate the presence and evolution of IR in patients with AI between 2003-2014 and to evaluate cortisol secretion over time and identify possible associations with clinical and biochemical parameters, in the context of IR.

METHODS

- Seventy three patients with AI and at least 3-year follow-up were included.
- Clinical examination, basal and dynamic adrenal testing to determine autonomous cortisol secretion (low dose dexamethasone suppression test, LDDST), biochemical investigation including a 75g Oral Glucose Tolerance Test to determine IR indices (HOMA, QUICKI, MATSUDA) and adrenal CT scan were performed.
- Patients' data were analyzed at baseline and at last follow-up.
- Pheochromocytomas, aldosterone secreting adenomas and adrenocortical carcinomas were excluded.
- Subtle autonomous cortisol secretion (SCAI) were considered at F <50 nmol/L (1.8 μg/dl) following LDDST.
- IR was define at HOMA>2.16 and QUICKI<0.34.
- Diabetes mellitus (T2DM) was considered when fasting glucose >126mg/dl or glucose after OGTT >200mg/dl.

variables	AI at baseline	AI at follow-up	*p* value
N (males)	73 (22)	73(22)	
Age (years)	57.2±9.0	62.7±8.8	<0.001
BMI (Kg/m2)	28.6±5.2	29.1±5.9	0.02
Waist (cm)	95.9±11.2	97.7±12.6	0.001
AI max size	2.1±0.8	2.3±0.8	<0.001
Hypertension	47	55	<0.001
dyslipidemia	24	40	<0.001
DM	2	9	<0.001
IGT	19	24	<0.001
IR	36	50	<0.001
HbA1c	5.2±0.5	5.6±0.6	<0.001
Fasting glucose (mg/dl)	87.7±11.3	94.6±13.4	<0.001
Fasting insulin(μIU/ml)	11.3±4.8	16.3±16.8	<0.001
HOMA-IR (mg/L)	2.50±1.2	3.9±4.2	<0.001
QUICKI	0.34±0.02	0.32±0.02	<0.001
MATSUDA	4.5±2.4	3.2±1.7	<0.001
Morning F (nmol/L)	432.6±177.8	438.7±149.7	0.73
ACTH (pg/ml)	18.9±10.8	16.6±9.9	0.04
UFC (μg/24h)	64.6±34.7	69.9±46.0	0.35
DHEA-S (ng/ml)	848.9±799	761.6±582.8	0.02
F post-LDDST (nmol/L)	45.1±31.4	64.8±55.7	<0.001
aldo(pmol/L)	232.4±115.9	277.0±194.4	0.2
Ren (mU/L)	9.8±5.7	8.9±7.8	0.02

Table1: Baseline and follow-up parameters

	BASELINE			FOLLOW-UP			Comparison between BASELINE and FOLLOW-UP	
VARIABLES	NFAI	CSAI	*p*1	NFAI	CSAI	*p*2	*p*3	*p*4
N (males)	53(15)	20(8)						
Age (years)	56.7±8.9	58.4±9.5	0.50	62.5±8.6	63.4±9.7	0.70	<0.001	<0.001
BMI (Kg/m2)	28.2±5.1	29.7±5.7	0.30	28.9±5.6	29.8±6.7	0.58	0.006	0.77
Waist (cm)	95.4±11.9	97.1±9.2	0.57	97.3±12.7	98.8±12.7	0.70	<0.001	0.29
AI max size	2.0±0.7	2.5±0.9	0.028	2.2±0.8	2.7±0.7	0.008	<0.001	0.049
Hypertension	31	16	0.10	37	18	0.13	<0.001	0.032
dyslipidemia	17	6	1.0	26	13	0.3	<0.001	0.05
DM	1	1	0.5	5	4	0.4	<0.001	0.009
IGT	13	6	0.5	17	7	0.4	<0.001	0.007
IR	22	14	0.04	31	19	0.002	<0.001	0.30
HbA1c (%)	5.1±0.5	5.3±0.6	0.16	5.5±0.6	5.8±0.52	0.13	<0.001	<0.001
Fasting glucose (mg/dl)	86.2±11.8	91.8±8.7	0.03	92.6±13.3	99.9±12.2	0.034	<0.001	0.001
Fasting insulin (μIU/ml)	10.5±4.2	13.6±5.5	0.023	12.9±4.9	25.3±29.8	0.002	<0.001	<0.001
HOMA-IR (mg/L)	2.5±1.0	3.1±1.4	0.011	3.0±1.4	6.3±7.3	0.002	<0.001	0.001
QUICKI	0.34±0.02	0.33±0.02	0.03	0.33±0.02	0.30±0.02	0.001	<0.001	<0.001
MATSUDA	4.8±2.6	3.5±1.5	0.008	3.6±1.8	2.3±1.0	0.001	<0.001	<0.001
Morning F (nmol/L)	421.2±166.9	462.8±205.5	0.42	411.5±135.2	510.1±165.6	0.23	0.6	0.25
ACTH (pg/ml)	20.7±11.6	14.1±6.4	0.007	17.9±10.8	12.6±5.4	0.019	0.029	0.514
UFC (μg/24h)	57.5±30.0	82.6±39.9	0.017	70.4±51.7	68.7±27.4	0.85	0.046	0.21
DHEA-S (ng/ml)	907.7±877.5	703.0±497.3	0.4	757.9±614.0	770.4±516.6	0.74	0.001	0.654
F post-LDDST (nmol/L)	30.4±9.7	84.0±36.0	<0.001	53.7±50.8	94.4±58.5	<0.001	<0.001	0.71
Aldo (pmol/L)	226.4±100.8	248.4±150.6	0.96	242.0±168.8	369.9±229.7	0.006	0.834	0.03
Ren (mU/L)	9.6±5.8	10.1±5.5	0.58	8.7±7.0	9.4±10.0	0.59	0.165	0.054

Table 2: Baseline and follow-up parameters of the patients with NFAI and CSAI (*p*1: NFAI *vs* CSAI at baseline, *p*2:NFAI *vs* CSAI at follow-up, *p*3: NFAI at baseline *vs* NFAI at follow- up and *p*4: CSAI at baseline *vs* CSAI at follow-up).

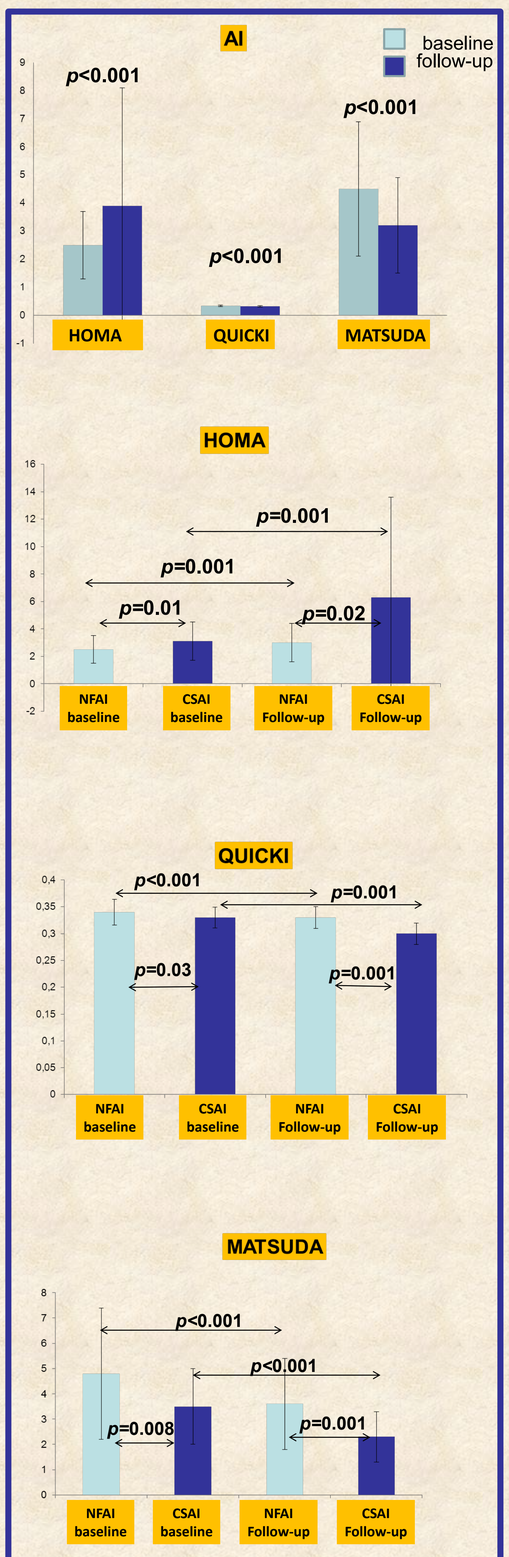

Fig 1: Indices of IR at diagnosis and follow-up.

RESULTS

During the follow-up (5.60±1.74years):

- the AI max diameter was increased however, less than 0.5cm; body mass index and waist circumference increased.
- 11% of the patients developed hypertension, 22% dyslipidemia, 9.6% T2DM and 19.2% IR (Table 1).
- At baseline, 20 patients had subtle autonomous cortisol secretion (CSAI) whereas 31 at last follow-up.

Categorizing the patients in NFAI and CSAI:

- T2DM developed in 7.5% of patients with non-functioning AI (NFAI) and 15% with CSAI.
- At baseline, 41.5% of NFAI and 70% of CSAI patients had IR, compared to 58.5% of NFAI and 95% of CSAI at the last follow-up (Table 2).
- IR indices values were higher both at diagnosis and last follow-up in patients with CSAI compared to NFAI (Fig 1).
- There was a positive correlation between post-dexamethasone cortisol levels (F-post-LDDST), HOMA and AI size and negative correlation between F-post-LDDST, QUICKI and MATSUDA in the whole group of patients both at baseline and at the last follow-up (Fig 2).

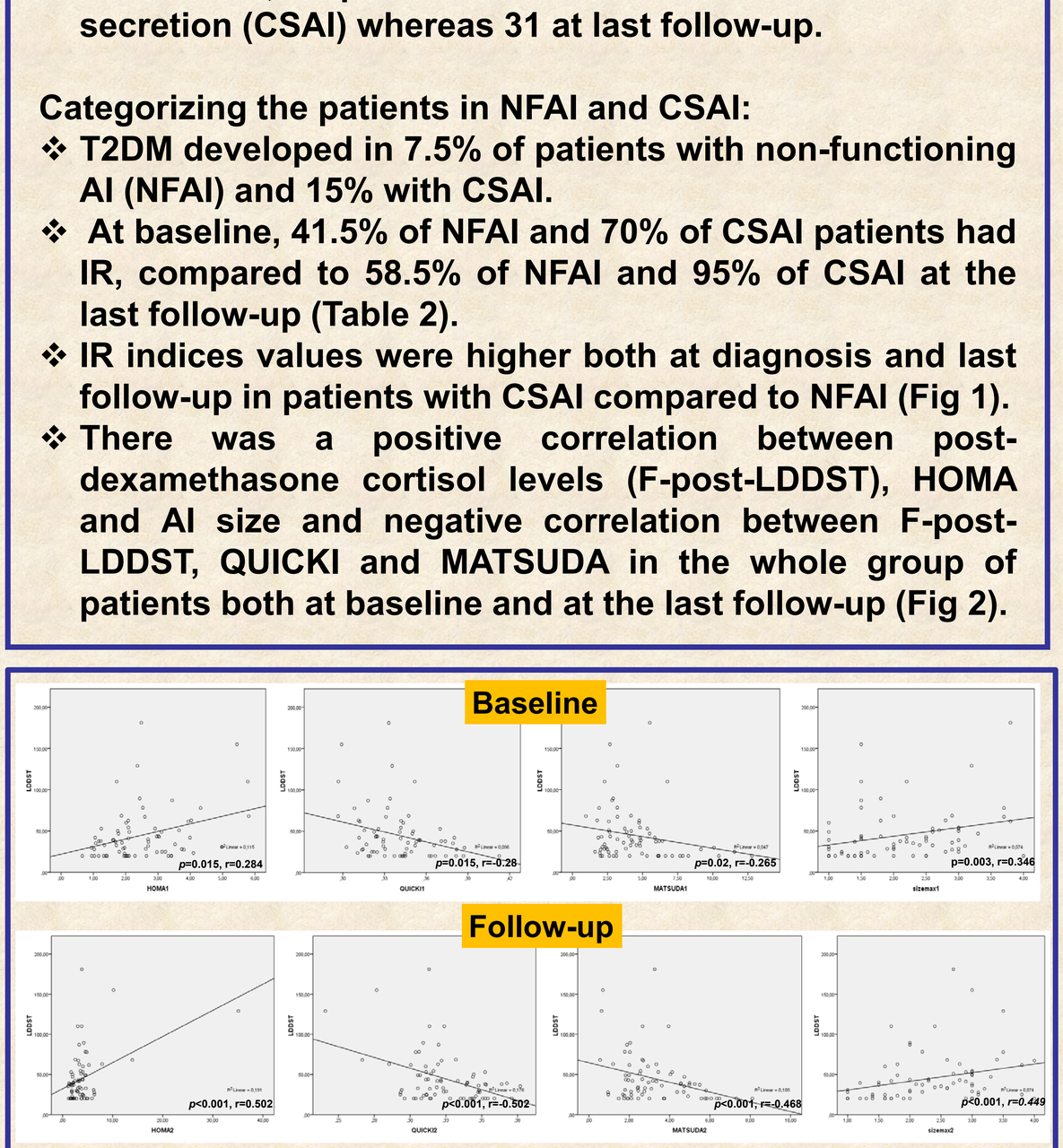

Fig 2: Correlations between F-post-LDDST, indices of IR and AI size.

CONCLUSIONS

During follow-up, autonomous cortisol secretion developed in 11 (15%) patients with initially NFAI. Apparently NFAI, as well as CSAI, exhibit deterioration of carbohydrates' metabolism and IR over a >3years' follow-up that correlate with the F-post-LDDST levels.

REFERENCES

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