Endothelial damage and thrombotic response in patients with cured Cushing Syndrome

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Background

Clinical observational studies have reported the persistence of a high cardiovascular risk in patients with cured Cushing's Syndrome (CCS) compared with controls of the same age, gender and body mass index (BMI). It is still at debated whether this is due to the persistence of comorbidities, hormone deficiencies or chronic changes induced by hypercortisolism.

Aim

To investigate the interplay in CCS of the cardiovascular disease in vivo and the endothelial activation and thrombogenicity in vitro occurring in response to sera of CCS.

Methods

Cross-sectional study in CS patients and controls and in vitro endothelial damage atherothrombotic model.

Subjects:

I. **CCS** (n:10) at minimun 2 years after cure and without hormone deficiencies.
II. **Active CS (ACS)** (n:10).
III. **Controls (CTR)** (n:10) matched for age, sex, sexual hormonal status, BMI and cardiometabolic profile.

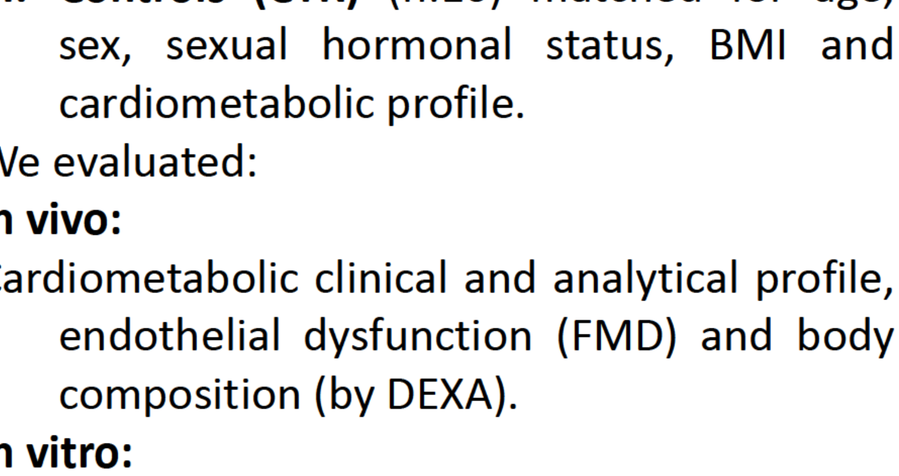
We evaluated:

In vivo:

Cardiometabolic clinical and analytical profile, endothelial dysfunction (FMD) and body composition (by DEXA).

In vitro:

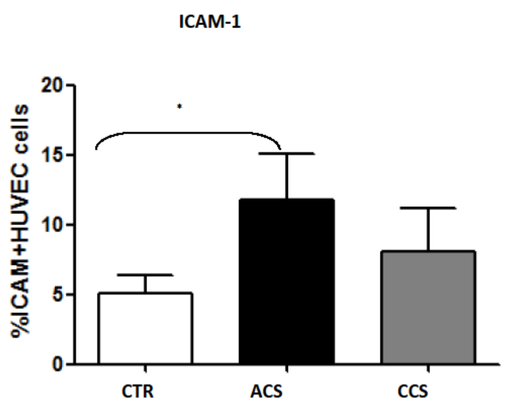
Endothelial cells (EC) were exposed for 24hs or have been cultured for 7 days with the differents sera (groups I, II, III) to evaluate the inflammatory EC response (VCAM, ICAM, NfKB) and the reactivity (vWF) of the extracellular matrix (ECM).

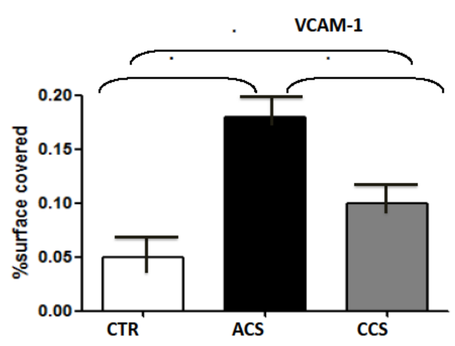


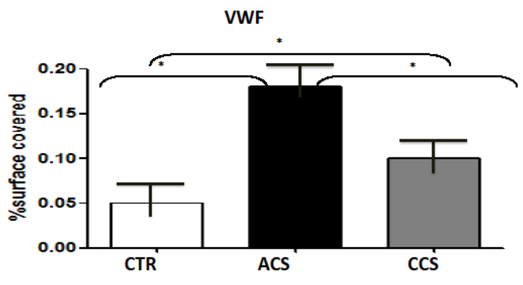
Results

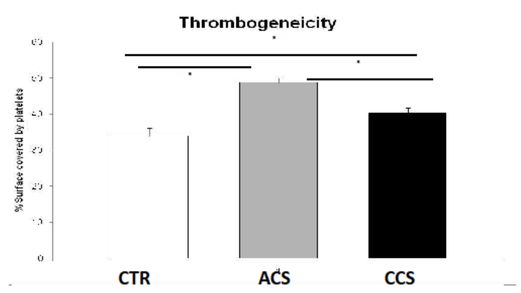
Baseline Parameters	ACS (n:10)	CCS (n:10)	CTR (n:10)	P value
Age (years)	37.8±5.7	37.3±6.7	38.3±6.4	0.947
Sex (M/F)	2/8	2/8	2/8	1
BMI (Kg/m2)	26.5±2.1	26.7±3.5	25.6±3.7	0.761
WC (cm)	91.5±13.8	87.1±13.9	81.6±12.3	0.390
Ratio WH	0.9±0.1	0.8±0.1	0.7±0.1	0.447
T2DM (%)	2(6.6)	0%	0%	0.159
HTA (%)	4(13.3)	2(6.6)	1%	0.289
DLP (%)	1(3.3)	1(3.3)	0%	0.501

Metabolic parameters	ACS (n:10)	CCS (n:10)	CTR (n:10)	P value
Glucose (mg/dl)	103.0±22.5	88.3±7.6	96.0±11.6	0.220
HbA1C (DCCT)	6.2±0.8	4.9±0.1	5.4±0.3	0.009
TC (mg/dl)	182.1±31.8	189.4±26.1	176.0±18.5	0.653
LDL (mg/dl)	105.1±24.1	117.0±23.0	98.5±23.9	0.370
HDL (mg/dl)	54.4±11.6	55.8±13.4	70.6±25.8	0.169
TG (mg/dl)	102.3±51.7	92.5±36.8	86.0±53.7	0.788
UsRCP (mg/dl)	0.22±0.09	0.11±0.04	0.08±0.07	0.001
Leucocytes (mm3)	8590.0±1475.3	6857.1±1407.0	5922.8±1497.5	0.004









ACS patients have a clinical, subclinical and in vitro proatherothrombotic phenotype. EC exposed to CCS sera displayed augmented expression of ICAM1 (p=0.06), VCAM (p=0.05), a higher synthesis of sub-endothelial vWF (p=0.03) and higner EC reactivity towards circulating platelets: platelets adhesion than CTRs of the same sex, age and BMI (p=0.04). NFkB is activated downstream.

Conclusions

This is the first translational study demostrating that the sera of patients with CCS have a deleterious atherothrombotic NFkB dependent potency on the endothelium inducing endothelial inflammatory activation and increased thrombogenicity.

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