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## Introduction

Cardiovascular disease is a major cause of death in patients with Cushing's syndrome (CS), either during active disease or after remission. Cardiac magnetic resonance (CMR) is currently regarded as the gold standard method for measuring structural and functional changes, with higher interstudy reproducibility and lower variability compared to 2-D echocardiography. In the present study, we aimed to investigate the metabolic profile and to detect the cardiac alterations through CMR in CS patients.

## Material and Methods

This was a prospective multicentric case-control study. Consecutive patients with CS both cured and with active disease, screened in the ERGO study (EudraCT number: 2015-004497-15) by two Italian referral centers, were enrolled. The control group consisted of sex, age, and BMI matched patients with non-functioning adrenal incidentaloma. Metabolic, clinical and cardiac parameters evaluated through CMR were assessed and compared in the two groups. Parametric and non-parametric tests were performed, as appropriate.

## Results

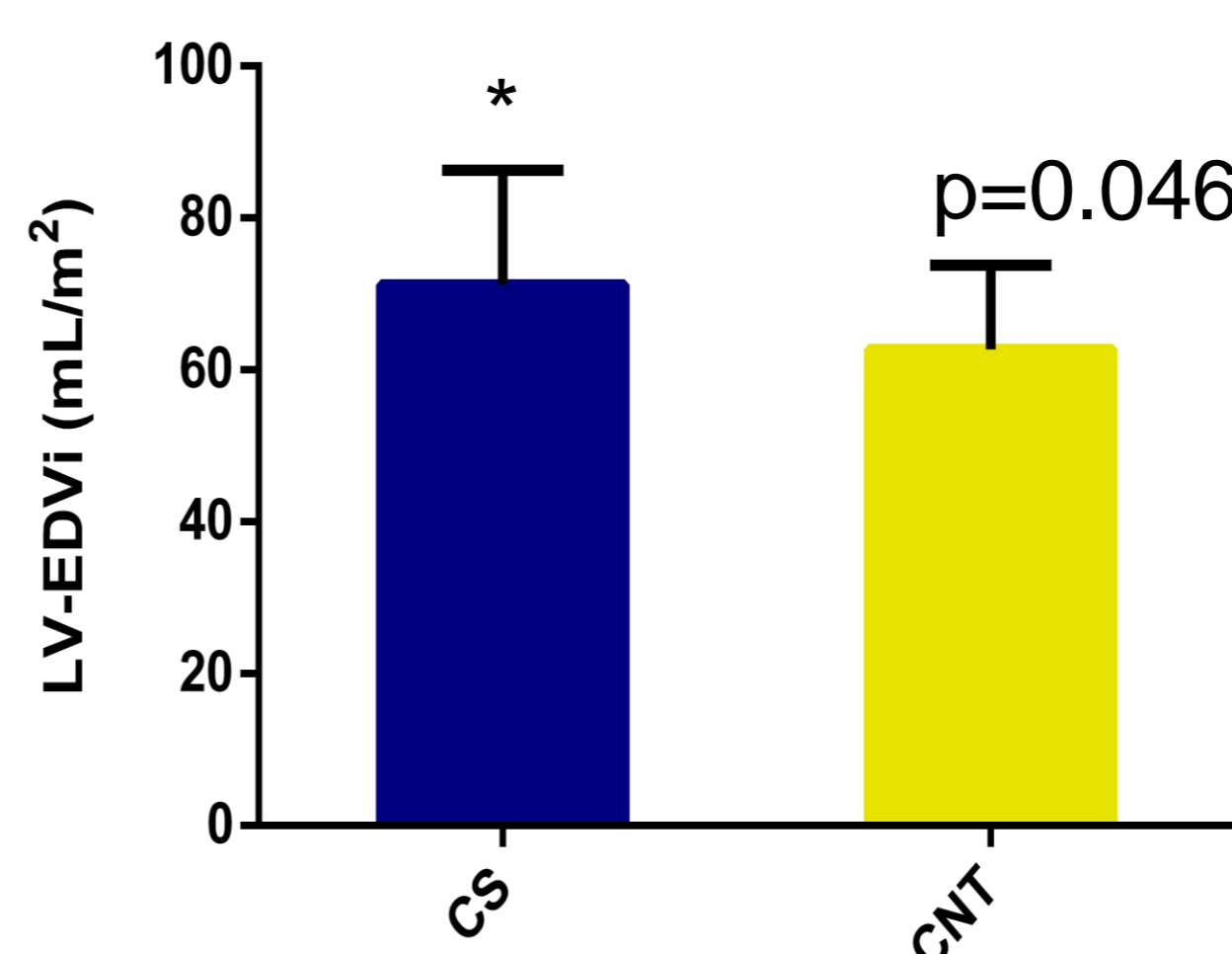
Sixteen patients with CS (12 females, 4 males) with a mean age of 48 years (range 20-71 years) and 18 matched controls entered the study. No significant differences were found neither in glucose and lipid levels, in systolic and diastolic blood pressure levels, nor in the prevalence of cardiometabolic complications.

LV end-diastolic volume (LV-EDV), LV end-diastolic volume indexed to the body surface (LV-EDVi), LV end-systolic volume (LV-ESV) and LV-ESVi were significantly higher in CS patients than controls ( $p=0.034$ ;  $p=0.046$ ;  $p=0.043$ ;  $p=0.014$ ), as well as indexed left ventricular mass (LVMi,  $p=0.042$ ). Right ventricle end-diastolic volume (RV-EDV), RV-EDVi, RV-ESV and RV-ESVi were also significantly higher in CS patients than controls ( $p=0.026$ ;  $p=0.013$ ;  $p=0.007$ ;  $p=0.003$ ), with a trend toward lower RV-EF in patients than controls ( $p=0.055$ ).

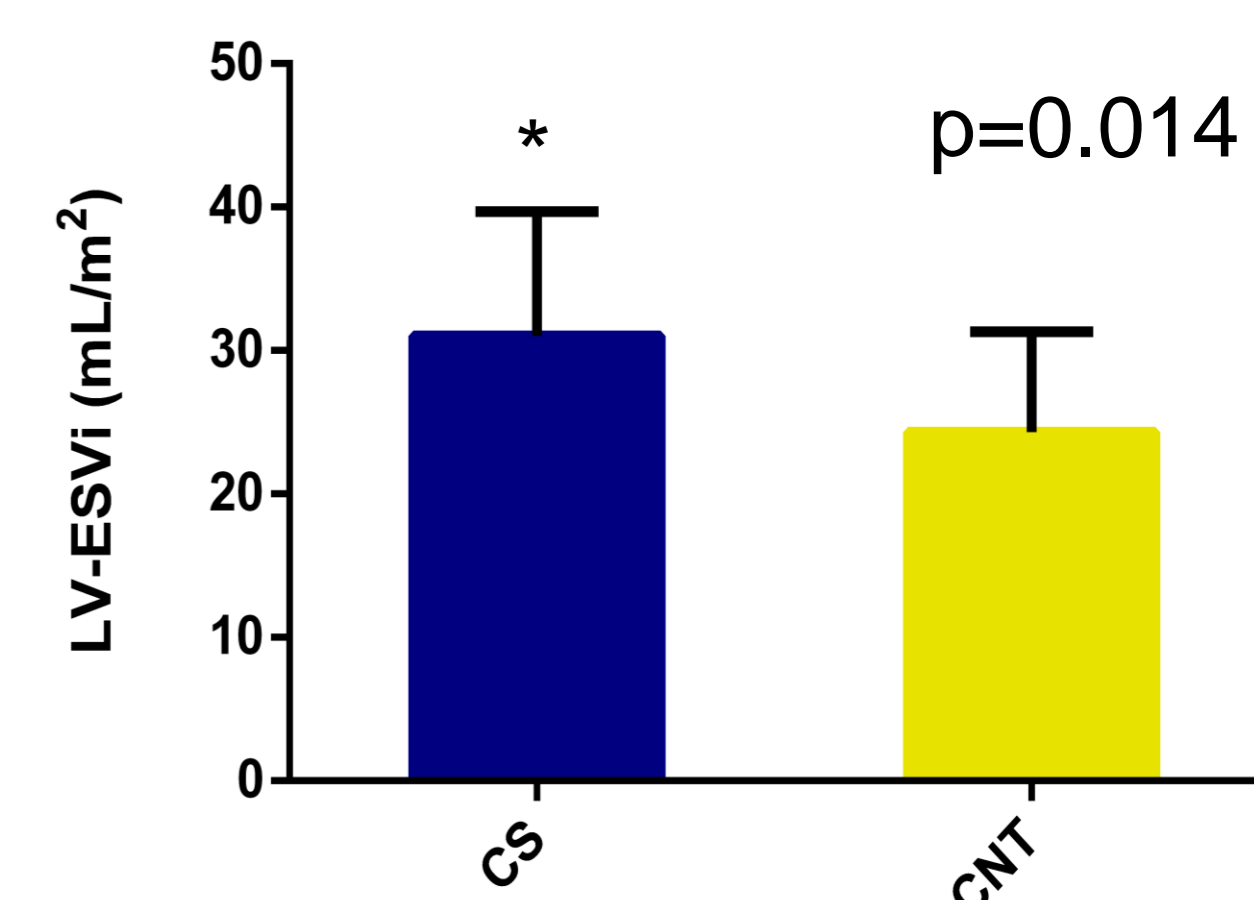
Parameters	CS patients n = 16	Controls n = 18	P value
LV-EDV (mL)	128.4 (112.3-142.3)	109.7 (95.0-167.7)	0.034
LV-EDVi (mL/m <sup>2</sup> )	71.2±15.1	62.7±11.1	0.046
LV-ESV (mL)	58.7±20.1	45.8±15.6	0.043
LV-ESVi (mL/m <sup>2</sup> )	31.0±8.7	24.3±7.0	0.014
LV-SV (mL)	71.6 (68.3-86.6)	71.3 (51.0-99.1)	0.601
LV-SVi (mL/m <sup>2</sup> )	39.2 (34.8-43.5)	36.8 (27.4-50.2)	0.418
LV-EF (%)	55.5 (53.3-61.6)	62.1 (52.0-70.4)	0.117
LVM (g)	90.8 (74.2-114.9)	85.1 (68.8-102.5)	0.160
LVMi (g/m <sup>2</sup> )	51.0±11.8	44.6±7.3	0.042
LVH (yes/no) (%)	0/16 (0%)	1/17 (5.5%)	0.741
Concentricity index (g/mL)	0.70±0.12	0.74±0.18	0.843
IVS-thickness (mm)	10.0 (8.2-12.7)	10.0 (7.0-13.4)	0.726
RV-EDV (mL)	134.9 (116.5-166.6)	117.0 (88.0-148.3)	0.026
RV-EDVi (mL/m <sup>2</sup> )	74.8±14.2	63.4±9.6	0.013
RV-ESV (mL)	63.7 (48.9-78.2)	51.3 (27.0-61.9)	0.007
RV-ESVi (mL/m <sup>2</sup> )	34.0±7.7	25.8±6.3	0.003
RV-SV (mL)	76.4±17.1	70.5±15.8	0.321
RV-SVi (mL/m <sup>2</sup> )	40.8±8.7	37.9±7.6	0.329
RV-EF (%)	54.6±5.5	59.3±7.7	0.055
T1-preMean (ms)	1003.4±25.0	997.1±18.7	0.522
T1-postMean (ms)	443.0±60.5	408.8±42.9	0.076
ECV (30%)	25.1±2.3	25.9±2.1	0.289
ECV>30% (yes/no)/(%)	0/16 (0%)	1/18 (5%)	0.341

### Cardiac parameters in CS patients and controls.

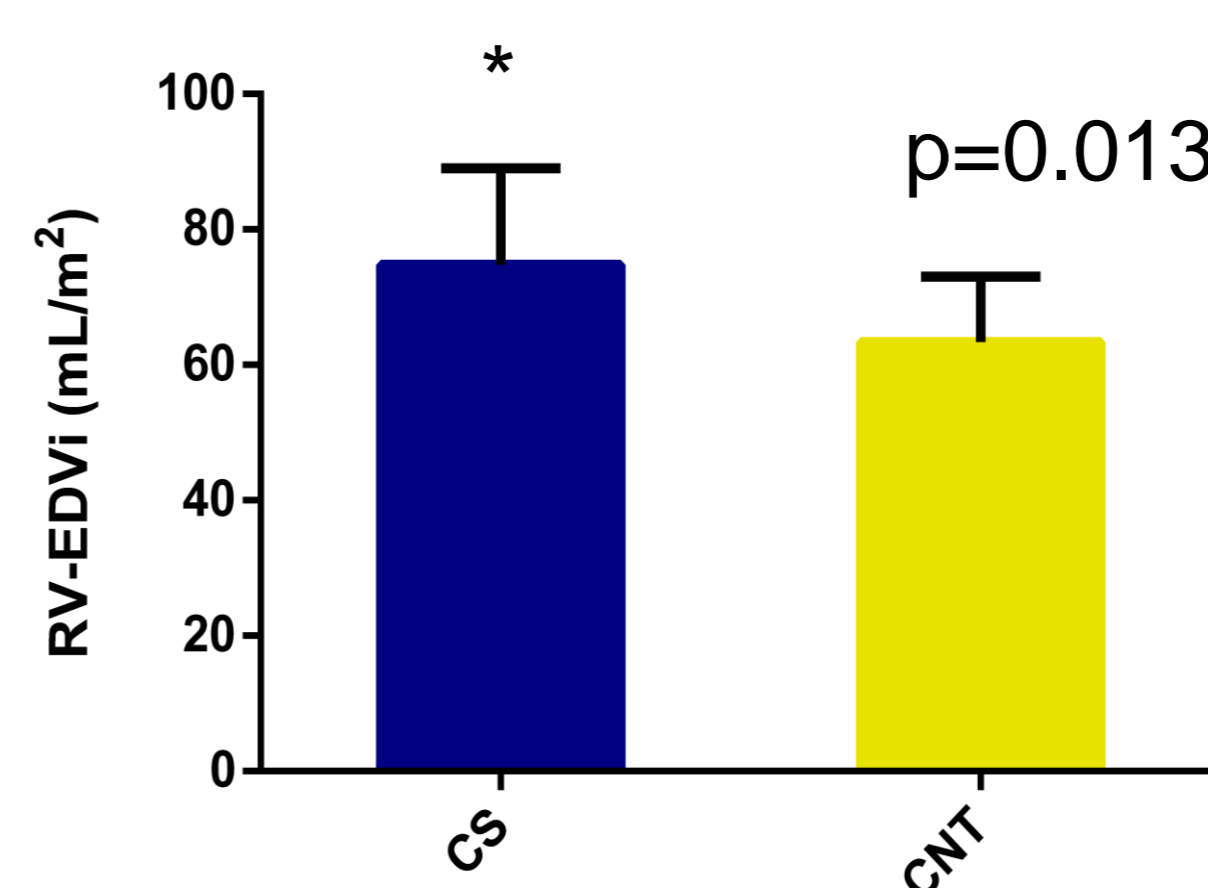
CS: Cushing's syndrome; n: number; LV: left ventricle; EDV: end-diastolic volume; EDVi: end-diastolic volume indexed; ESV: end-systolic volume; ESVi: end-systolic volume indexed; SV: stroke volume; SVi: stroke volume indexed; EF: ejection fraction; LVM: left ventricular mass; LVMi: left ventricular mass indexed; LVH: left ventricular hypertrophy; IVS: interventricular sept; RV: right ventricle; ECV: extra-cellular volume



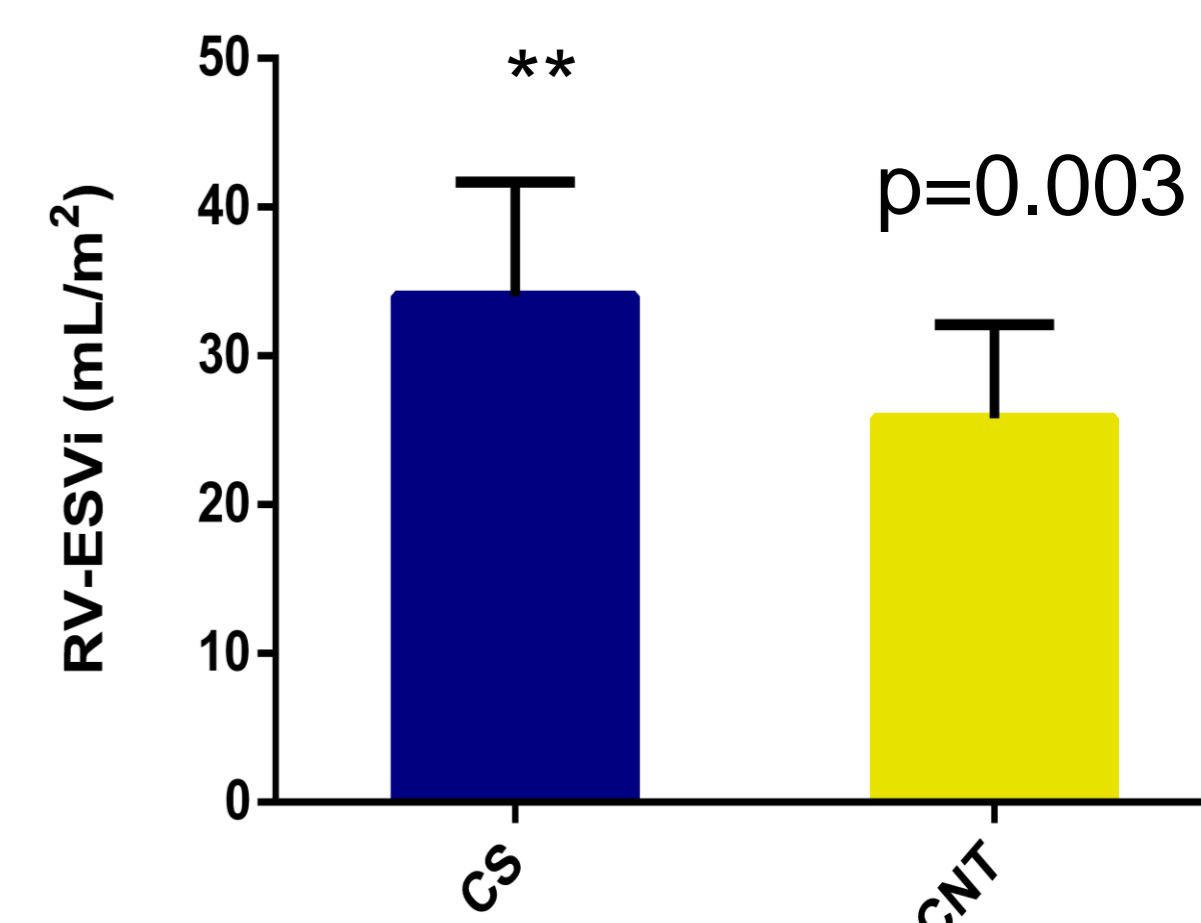
Mean LV-EDVi in CS patients and controls.



Mean LV-ESVi in CS patients and controls.



Mean RV-EDVi in CS patients and controls.



Mean RV-ESVi in CS patients and controls.

## Discussion

CS patients present with biventricular cardiac structural and functional impairment at CMR, which seem to derive from a direct effect of hormone excess, determining changes in cardiac muscle, independently from the presence of disease-related cardiovascular risk factors (such as hypertension, visceral obesity, metabolic impairment), which role need further investigations. Our study suggests that CMR may have a place in the cardiac work-up of selected patients with CS.

References: 1. Pivonello R, Isidori AM, De Martino MC, Newell-Price J, Biller BMK, Colao A. Lancet Diabetes Endocrinol 2016; 4: 611-29.  
2. Grothues F, Smith GC, Moon JC, et al. Am J Cardiol. 2002; 90:29-34.

The authors have no conflict of interest to declare.