

SUPPLEMENTARY MATERIAL

Supplementary Table 1. Questionnaire.

Survey on Management of Hypercortisolism and Cushing's Syndrome
(1) <i>What is your specialty?</i> a) Internal Medicine b) Nephrology c) Cardiology d) Endocrinology e) Other, specify
(2) <i>What is the average number of patients with hypertension seen in your service/centre in 1 year?</i>
(3) <i>How many patients are seen as first visit?</i>
(4) <i>What is the percentage of patients with resistant hypertension seen in your service/centre?</i>
(5) <i>How many cases of Cushing syndrome were diagnosed in the last 5 years in your service/centre? (of which Pituitary N=.....; Adrenal N=.....; other N=.....)</i>
(6) <i>In which group of patients, you request the evaluation of 24h urinary free cortisol or the overnight 1-mg dexamethasone suppression test if not performed before?</i> a) Patients with hypertension and specific features (buffalo hump, moon facies, purple reddish striae) b) All patients with diabetes and hypertension c) All patients with hypertension and adrenal mass d) All patients with hypertension and obesity e) All patients with hypertension and obesity and adrenal mass f) All patients with resistant hypertension g) All patients with hypertension aged less than 50 years h) When the phenotype is suspect, I refer the patient to an endocrinologist for further investigations
(7) <i>Which test(s) do you perform for screening of hypercortisolism?</i> a) 1-mg overnight dexamethasone suppression test b) 24h urinary free cortisol c) Late night salivary cortisol d) Basal cortisol and ACTH e) Adrenal CT scanning or MRI f) I refer to the endocrinologist without performance of any test
(8) <i>Are you aware of a referral centre in your area with expertise of Cushing syndrome management?</i>
(9) <i>How do you consider a patient with a level of cortisol of 2.5 µg/dL at 8 a.m. after overnight 1-mg dexamethasone suppression test?</i> a) Positive b) Negative c) Grey zone, I request further tests (please describe) d) I refer to an endocrinologist
(10) <i>How many patients with subclinical hypercortisolism (mild autonomous cortisol secretion) did you diagnose in the last 5 years?</i>

The table reports the 10-items questionnaire designed for physicians treating patients with hypertension to investigate current screening methods for hypercortisolism.

Supplementary Table 2. Number of patients according to geographical area, prevalent medical specialty, and excellence centers.

Geographical Areas	North (n=52)	Centre-South (n=30)	P-value	
Average number of referred patient in 1 year (n)	600 [300; 1338]	675 [300; 2000]	0.585	
Patients evaluated as first visit (n)	175 [100; 300]	175 [50; 500]	0.828	
Patients with resistant hypertension (%)	10.0 [5.0; 28.8]	12.5 [5.0; 20.0]	0.919	
Cases of Cushing syndrome in the last 5 years (n)	1 [0; 4]	2 [0; 6]	0.658	
Cases of MACS in the last 5 years (n)	1 [0; 4]	0 [0; 3]	0.207	
Prevalent Specialty	Internal Medicine (n=36)	Cardiology (n=25)	Others* (n=21)	P-value
Average number of referred patient in 1 year (n)	600 [300; 1876]	800 [300; 1425]	500 [175; 1650]	0.731
Patients evaluated as first visit (n)	225 [105; 463]	150 [80; 350]	100 [30; 275]	0.064
Patients with resistant hypertension (%)	12.5 [6.3; 30.0]	10.0 [5.0; 12.5]	15.0 [10.0; 45.0]	0.048
Cases of Cushing syndrome in the last 5 years (n)	3 [1; 7]	0 [0; 2]	1 [0; 5]	0.009
Cases of MACS in the last 5 years (n)	1 [0; 10]	0 [0; 2]	0 [0; 4]	0.222
Excellence Centres	Yes (n=25)	No (n=57)	P-value	
Average number of referred patient in 1 year (n)	1500 [500; 2000]	450 [200; 1000]	<0.001	
Patients evaluated as first visit (n)	300 [175; 650]	100 [60; 300]	<0.001	
Patients with resistant hypertension (%)	15.0 [6.5; 30.0]	10.0 [5.0; 22.5]	0.895	
Cases of Cushing syndrome in the last 5 years (n)	3 [1; 9]	0 [0; 3]	0.001	
Cases of MACS in the last 5 years (n)	2 [1; 15]	0 [0; 2]	<0.001	

The table reports number of referred patients with Cushing syndrome or subclinical hypercortisolism (MACS) after stratification for geographical areas, prevalent medical specialty, and type of centre. Data are reported as median [interquartile range]. *Others: endocrinology, nephrology, geriatrics. *P*-value < 0.05 were considered significant and highlighted in bold.

Supplementary Table 3. Management of hypercortisolism and Cushing's syndrome according to geographical areas.

Geographical Areas	North (n=52)	Centre-South (n=30)	P-value
<i>(6) In which group of patients, you request the evaluation of 24h urinary free cortisol or the overnight 1-mg dexamethasone suppression test if not performed before?</i>			
a) Patients with hypertension and specific features	40 (76.9)	23 (76.7)	1.000
b) All patients with diabetes and hypertension	4 (7.7)	2 (6.7)	1.000
c) All patients with hypertension and adrenal mass	32 (61.5)	23 (76.7)	0.160
d) All patients with hypertension and obesity	9 (17.3)	0 (0.0)	0.023
e) All patients with hypertension and obesity and adrenal mass	19 (36.5)	12 (40.0)	0.752
f) All patients with resistant hypertension	30 (57.7)	20 (66.7)	0.424
g) All patients with hypertension aged less than 50 years	18 (34.6)	8 (26.7)	0.454
h) When the phenotype is suspect, I refer the patient to an endocrinologist	10 (19.2)	3 (10.0)	0.356
<i>(7) Which test(s) do you perform for screening of hypercortisolism?</i>			
a) 1-mg overnight dexamethasone suppression test	28 (53.8)	12 (40.0)	0.227
b) 24h urinary free cortisol	30 (57.7)	24 (80.0)	0.054
c) Late night salivary cortisol	6 (11.5)	3 (10.0)	1.000
d) Basal cortisol and ACTH	24 (46.2)	20 (66.7)	0.073
e) Adrenal CT scanning or MRI	6 (11.5)	4 (13.3)	1.000
f) I refer to the endocrinologist without performance of any test	7 (13.5)	3 (10.0)	0.739
<i>(8) Are you aware of a referral centre in your area with expertise of Cushing syndrome management?</i>			
a) Yes	35 (67.3)	22 (73.3)	0.566
b) No	17 (32.7)	8 (26.7)	
<i>(9) How do you consider a patient with a level of cortisol of 2.5 µg/dL at 8 a.m. after overnight 1-mg dexamethasone suppression test?</i>			
a) Positive	8 (15.4)	4 (13.3)	1.000
b) Negative	0 (0.0)	4 (13.3)	0.016
c) Grey zone, I request further tests	22 (42.3)	11 (36.7)	0.617
d) I refer to an endocrinologist	22 (42.3)	11 (36.7)	0.617

Responses to questions 6-to-9 of the questionnaire after stratification for geographical areas. Data are reported as absolute numbers and frequencies, as appropriate. *P*-value < 0.05 were considered significant and highlighted in bold.

Supplementary Table 4. Management of hypercortisolism and Cushing's syndrome according to type of centre (excellent vs non excellent).

Excellence Centres	Excellent Centres (n=25)	Non Excellent Centres (n=57)	P-value
<i>(6) In which group of patients, you request the evaluation of 24h urinary free cortisol or the overnight 1-mg dexamethasone suppression test if not performed before?</i>			
a) Patients with hypertension and specific features	20 (80.0)	43 (75.4)	0.655
b) All patients with diabetes and hypertension	3 (12.0)	3 (5.3)	0.363
c) All patients with hypertension and adrenal mass	20 (80.0)	35 (61.4)	0.107
d) All patients with hypertension and obesity	3 (12.0)	6 (10.5)	1.000
e) All patients with hypertension and obesity and adrenal mass	11 (44.0)	20 (35.1)	0.442
f) All patients with resistant hypertension	17 (68.0)	33 (57.9)	0.386
g) All patients with hypertension aged less than 50 years	11 (44.0)	15 (26.3)	0.113
h) When the phenotype is suspect, I refer the patient to an endocrinologist	3 (12.0)	10 (17.5)	0.745
<i>(7) Which test(s) do you perform for screening of hypercortisolism?</i>			
a) 1-mg overnight dexamethasone suppression test	13 (52.0)	27 (47.4)	0.699
b) 24h urinary free cortisol	19 (76.0)	35 (61.4)	0.052
c) Late night salivary cortisol	3 (12.0)	6 (10.5)	1.000
d) Basal cortisol and ACTH	14 (56.0)	30 (52.6)	0.777
e) Adrenal CT scanning or MRI	3 (12.0)	7 (12.3)	1.000
f) I refer to the endocrinologist without performance of any test	2 (8.0)	8 (14.0)	0.501
<i>(8) Are you aware of a referral centre in your area with expertise of Cushing syndrome management?</i>			
a) Yes	25 (100.0)	32 (56.1)	<0.001
b) No	0 (0.0)	25 (43.9)	
<i>(9) How do you consider a patient with a level of cortisol of 2.5 µg/dL at 8 a.m. after overnight 1-mg dexamethasone suppression test?</i>			
a) Positive	6 (24.0)	6 (10.5)	0.172
b) Negative	1 (4.0)	3 (5.3)	1.000
c) Grey zone, I request further tests	13 (52.0)	20 (35.1)	0.150
d) I refer to an endocrinologist	5 (20.0)	28 (49.1)	0.013

Responses to questions 6-to-9 of the questionnaire after stratification according to type of centre. Data are reported as absolute numbers and frequencies, as appropriate. P-value < 0.05 were considered significant and highlighted in bold.