

Supplementary Table 1: Data categorized by history of pituitary or adrenal diseases.

Characteristic	With pituitary or adrenal diseases (n=240)	Without pituitary/adrenal disease (n=277)	P-value
Demographic data			
Age, (mean ±SD) (yr)	47.27±15.68	53.74±18.53	<0.001
- < 50 years old, n(%)	118 (49.17)	96 (34.66)	
- ≥ 50 years old, n(%)	122 (50.83)	181 (65.34)	0.001
Male, n(%)	128 (53.33)	124 (44.77)	0.052
Weight, (mean ±SD) (kgs)	63.37±14.74	58.20±15.64	0.002
BMI, (mean±SD)(kg/m ²)	23.00±6.46	24.76±6.12	0.001
ACTH stimulation dose, n(%)			
- 1 µg	77 (32.08)	114 (41.16)	
- 250 µg	163 (67.92)	163 (58.84)	0.033
Adrenal insufficiency, n(%)	50 (20.83)	78 (28.16)	0.054
Systolic blood pressure, (mean± SD) (mmHg)	122.69±19.49	120.26±21.19	0.178
Diastolic blood pressure, (mean± SD) (mmHg)	75.26±13.77	71.61±13.13	0.002
Underlying disease, n(%)			
- Diabetes mellitus	36 (15.00)	42 (15.22)	0.945
- Hypertension	49 (20.42)	75 (27.17)	0.073
- Chronic kidney disease	5 (2.08)	11 (3.97)	0.216
- Autoimmune disease	12 (5.00)	67 (24.19)	<0.001
- Cancer	1 (0.42)	15 (5.42)	0.001
Symptom, n(%)			
- Fatigue	24 (10.00)	83 (29.96)	<0.001
- Weight loss	4 (1.67)	22 (7.94)	0.001
- Orthostatic Hypotension	1 (0.42)	49 (17.96)	<0.001
- Nausea/vomiting	2 (0.83)	7 (2.53)	0.142
Cushingoid appearance in exogenous steroid use	2 (0.83)	64 (23.10)	<0.001
Biochemical values			
Serum morning cortisol (mean ±SD) (µg/dL)	9.20±3.44	9.02±3.13	0.537
< 9 µg/dL, n(%)	123 (51.25)	149 (53.79)	
≥ 9 µg/dL, n(%)	117 (48.75)	128 (46.21)	0.332
Serum basal cortisol (mean ±SD) (µg/dL)	9.60±4.55	9.69±5.71	0.839
< 9 µg/dL, n(%)	121 (50.42)	148 (53.43)	
≥ 9 µg/dL, n(%)	119 (49.58)	129 (46.57)	0.467
Serum K (mean ±SD) (mEq/L)	4.00±0.41	4.06±0.57	0.188
< 3 mEq/L, n(%)	5 (2.08)	32 (11.55)	
≥ 3 mEq/L, n(%)	235 (97.92)	245 (88.45)	<0.001
Serum Na (mean ±SD) (mEq/L)	137.75 (9.73)	138.84 (12.58)	0.269
< 135 mEq/L, n(%)	26 (10.83)	49 (17.69)	
≥ 135 mEq/L, n(%)	214 (89.17)	228(82.32)	0.027
Eosinophilia, n(%)	20 (11.63)	26 (11.40)	0.944
Lymphocytosis, n(%)	131 (54.58)	158 (57.04)	0.575
Serum albumin (mean±SD) (g/dL)	4.02±0.54	3.82±0.64	<0.001
< 3 g/dL	5 (2.08)	32 (11.55)	

Characteristic	With pituitary or adrenal diseases (n=240)	Without pituitary/adrenal disease (n=277)	P-value
≥ 3 g/dL	235 (97.92)	245 (88.45)	<0.001
Total cholesterol (mean±SD) (mg/dL)	188.04±43.65	177.32±55.50	0.016
< 150 mg/dL	203 (84.58)	194 (70.04)	
≥ 150 mg/dL	37 (15.42)	83 (29.96)	<0.001

Supplementary Table 2: Data categorized by primary or secondary adrenal insufficiency.

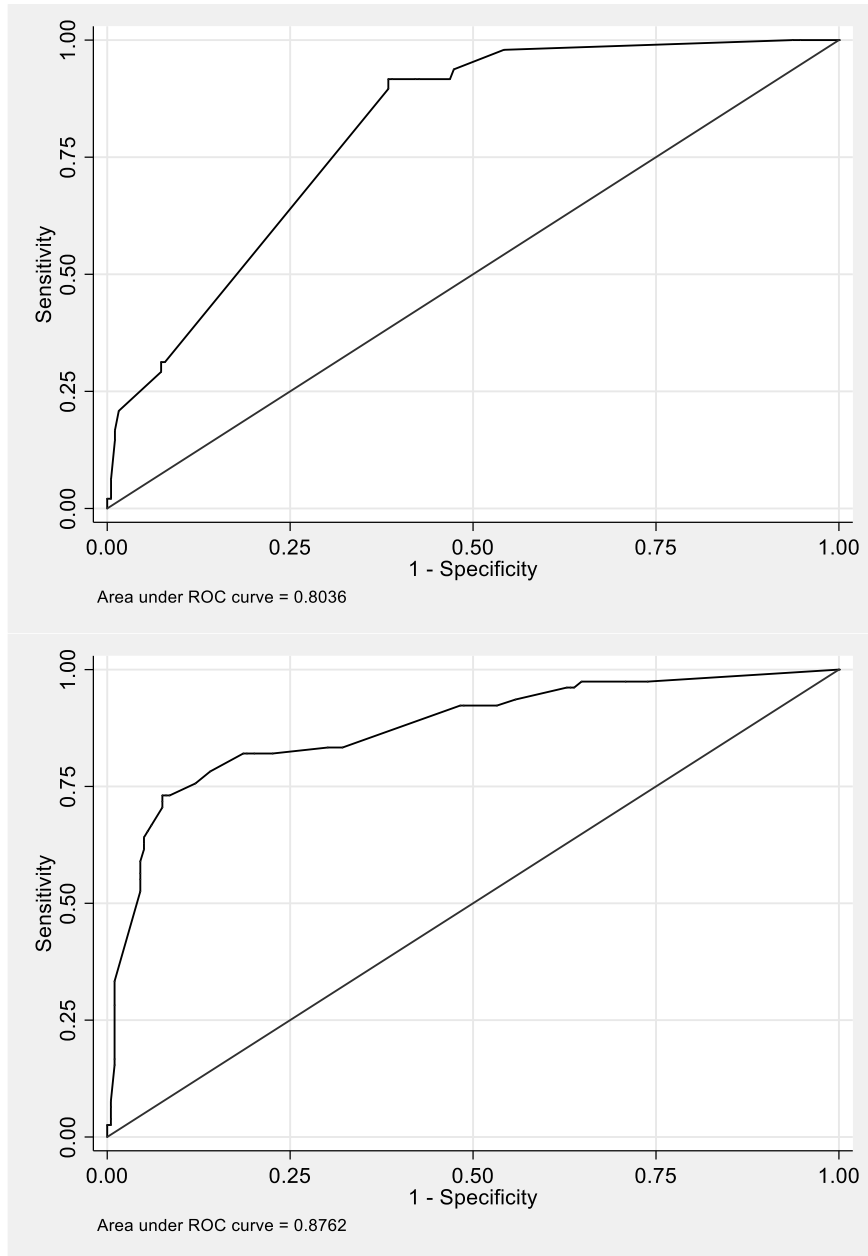
Characteristic	Primary adrenal insufficiency (n=18)	Secondary adrenal insufficiency (n=499)	P-value
Demographic data			
Age, (mean ±SD) (yr)	41.22±15.84	51.08±17.52	0.019
- < 50 years old, n(%)	12 (66.67)	202 (40.48)	
- ≥ 50 years old, n(%)	6 (33.33)	297 (59.52)	0.027
Male, n(%)	6 (33.33)	246 (49.30)	0.183
Weight, (mean ±SD) (kgs)	54.35±11.48	60.87±15.51	0.078
BMI, (mean±SD)(kg/m ²)	21.77±4.97	23.90±6.40	0.162
ACTH stimulation dose, n(%)			
- 1 µg	5 (27.78)	186 (37.27)	
- 250 µg	13 (72.22)	313 (62.73)	0.412
Systolic blood pressure, (mean± SD) (mmHg)	120.66±18.32	121.42±20.52	0.877
Diastolic blood pressure, (mean± SD) (mmHg)	69.99±18.03	73.43±13.25	0.290
Underlying disease, n(%)			
- Diabetes mellitus	3 (16.67)	75 (15.06)	0.852
- Hypertension	5 (27.78)	119 (23.90)	0.705
- Chronic kidney disease	0 (0.00)	16 (3.21)	0.440
- Autoimmune disease	0 (0.00)	79 (15.83)	0.067
- Cancer	0 (0.00)	16 (3.21)	0.440
Cushingoid appearance in exogenous steroid use	0 (0.00)	66 (13.23)	0.099
Biochemical values			
Serum morning cortisol (mean ±SD) (µg/dL)	8.67±3.61	9.12±3.27	0.678
< 9 µg/dL, n(%)	10 (55.56)	262 (52.51)	
≥ 9 µg/dL, n(%)	8 (44.44)	237 (47.49)	0.799
Serum basal cortisol (mean ±SD) (µg/dL)	8.74±4.98	9.68±5.21	0.816
< 9 µg/dL, n(%)	8 (44.44)	261 (52.30)	
≥ 9 µg/dL, n(%)	10 (55.56)	238 (47.70)	0.512
Serum K (mean ±SD) (mEq/L)	4.21±0.37	4.03±0.50	0.143
< 3 mEq/L, n(%)	0 (0.00)	6 (1.20)	
≥ 3 mEq/L, n(%)	18 (100.00)	493 (98.80)	0.640
Serum Na (mean ±SD) (mEq/L)	130.80 (31.86)	138.52 (9.53)	0.003
< 135 mEq/L, n(%)	3 (16.67)	72 (14.43)	
≥ 135 mEq/L, n(%)	15 (83.33)	427 (85.57)	0.791
Eosinophilia, n(%)	2 (11.11)	44 (11.31)	0.481
Lymphocytosis, n(%)	7 (38.89)	282 (56.51)	0.139
Serum albumin (mean±SD) (g/dL)	4.08±0.88	3.91±0.59	0.229
< 3 g/dL	1 (5.56)	36 (7.21)	
≥ 3 g/dL	17 (94.44)	463 (92.79)	0.789
Total cholesterol (mean±SD) (mg/dL)	169.29±50.67	182.76±50.67	0.267
< 150 mg/dL	5 (27.78)	115 (23.05)	
≥ 150 mg/dL	13 (72.22)	384 (76.95)	0.640

Supplementary Table 3: Performance capacity between serum morning and basal cortisol.

Model	ROC area	95%CI	P-value
Morning cortisol	0.65	0.60-0.70	
Basal cortisol	0.79	0.74-0.83	<0.0001

Supplementary Table 4: Multivariable risk regression of predictive factors for adrenal insufficiency clustered by ACTH dose categorized by patients with and without pituitary/adrenal diseases.

Patients without pituitary and adrenal diseases (n=277)				
Factor	RR	95%CI	P-value	
Chronic kidney disease	2.32	1.63-3.31	<0.001	
Cushingoid appearance in exogenous steroid and/or herbal medicine use	5.16	3.21-8.31	<0.001	
Nausea and/or vomiting	1.47	1.23-1.75	<0.001	
Fatigue	1.23	1.14-1.32	<0.001	
Serum basal cortisol <9 µg/dL	1.97	1.87-2.06	<0.001	
Cholesterol <150 mg/dL	1.38	1.19-1.60	<0.001	
Serum sodium <135 mEq/L	1.20	1.12-1.30	<0.001	
Patients with pituitary and adrenal diseases (n=240)				
Chronic kidney disease	5.07	1.92-13.35	0.001	
Cushingoid appearance in exogenous steroid and/or herbal medicine use	4.09	2.31-7.24	<0.001	
Nausea and/or vomiting	2.39	1.19-4.77	0.013	
Fatigue	2.40	1.28-4.50	0.006	
Serum basal cortisol <9 µg/dL	9.32	3.32-26.14	<0.001	
Cholesterol <150 mg/dL	1.24	1.04-1.47	0.016	
Serum sodium <135 mEq/L	0.72	0.56-0.93	0.011	



Supplementary Figure 1: Area under ROC of the predictive model for adrenal insufficiency categorized by those with or without pituitary or adrenal diseases. A) Area under ROC of the predictive model for adrenal insufficiency in patients without history of pituitary or adrenal diseases ($n=277$); B) Area under ROC of the predictive model for adrenal insufficiency in patients with history of pituitary or adrenal diseases ($n=240$).