Cushing Syndrome in Older Women: Age-Related Differences in Disease Origin and Clinical Manifestations

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Background

- ACTH-producing pituitary adenoma is the most common cause of endogenous Cushing syndrome. However, the relative proportion of adrenal causes of Cushing syndrome is rising.
- Limited data are available on the presentation and cause of Cushing syndrome in older women.

Study Objective: Determine the clinical presentation, biochemical profile, and cause of Cushing syndrome in women ≥65 years of age, compared with younger patients with Cushing syndrome

Methods

- Retrospective charts review of patients with Cushing syndrome from two electronic databases: Maccabi Healthcare Services (2000-2017) and the Endocrine Institute at Rabin Medical Center (2000-2020).
- Patients were classified into 3 groups, according to age at diagnosis:
  - Young: ≤45 years
  - Middle-aged: 46-64 years
  - Elderly: ≥65 years
- Outcomes of interest, according to age groups: (i) disease origin; (ii) reasons for investigation for hypercortisolism; (iii) biochemical profile.

Results

- Cohort consisted of 142 patients (mean age, 46.0±15.1 years).
- Pituitary source was most common among young women.
- Adrenal source was most common among elderly.
- Most elderly were diagnosed following workup for incidentaloma.
- Weight gain was common in young women, rare in elderly.
- Mean UFC levels were highest for young women or middle-aged women compared with elderly women (P < 0.001), while no difference was recorded for serum cortisol levels following 1 mg DST.
- There was no difference between groups in adrenal or pituitary tumor size.

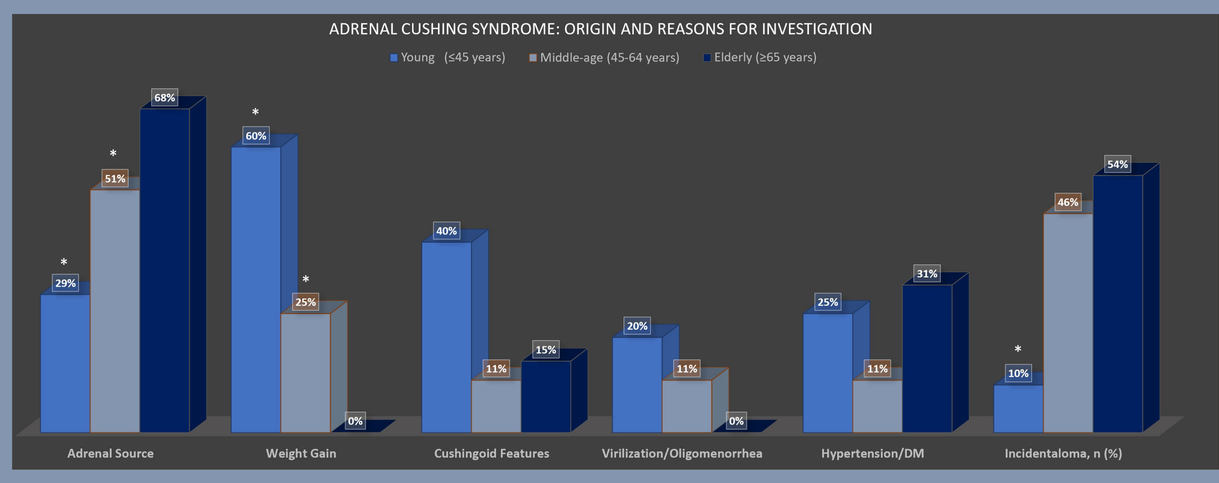
	Total	Young (≤45 years)	Middle-age (45-64 years)	Elderly (≥65 years)
Patients	**142**	68	55	19
Pituitary Source	**81 (57%)**	48 (71%)	27 (49%)	6 (32%)
Adrenal Source	**61 (43%)**	20 (29%	28 (51%)	13 (68%)

Baseline Characteristics			
	Young (≤45 years)	Middle-age (45-64 years)	Elderly (≥65 years)
Patients	68	55	19
Patient Characteristics			
Age , mean (median)	33.4 (36)*	53.2 (53)*	70.3 (69)
BMI (median)	30.0 (30.0)	33.9 (32.4)	27.5 (25.6)
Reason for Investigation			
Weight Gain	39 (57%)*	19 (35%)*	3 (16%)
Cushingoid Features	15 (22%)	11 (20%)	4 (21%)
Virilization	28 (41%)*	7 (13%)	1 (5%)
Hypertension/DM	16 (24%)	14 (26%)	6 (31%)
Adrenal Incidentaloma	3 (4%)*	15 (27%)	7 (37%)
Biochemical Data			
UFC, xULN, median (IQR)	3.8 (2.7-6.0)*	3.2 (2.3-4.4)*	2.3 (2.0-5.3)
Cortisol post LDDST, nmol/L,median (IQR)	396 (183-695)	439 (174-577)	423 (153-688)
Imaging Data			
Pituitary Adenoma Size, mm, median (IQR)	6 (5-10)	7 (4-13)	8 (6-9)
Adrenal Adenoma Size, mm, median (IQR)	34 (25-39)	32 (26-45)	38 (27-58)

Results – Cont.

- *Adrenal Source*:

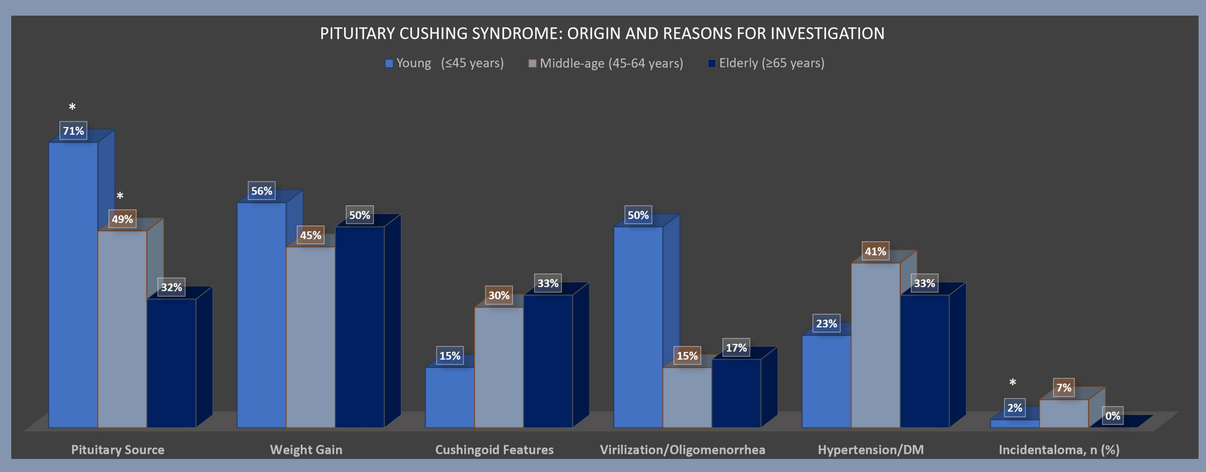
Adrenal Source			
	Young (≤45 years)	Middle-age (45-64 years)	Elderly (≥65 years)
Patients	20	28	13
Patient Characteristics			
Age , mean (median)	34.4 (38)	54.2 (54)	69.9 (68)
BMI, mean (median)	30.9 (30.4)	34.0 (31.4)	26.6 (25.8)
Biochemical Data			
UFC, xULN, median (IQR)	6.0 (3.8-9.9)*	2.4 (1.9-3.7)	2.2 (1.6-2.9)
Cortisol post LDDST, nmol/L,median (IQR)	664 (276-762)	537 (190-605)	292 (125-448)
ACTH, xULN, median (IQR)	0 (0-0)	0 (0-0)	0 (0-0)
Imaging Data			
Adenoma Size, mm, median (IQR)	34 (25-39)	32 (26-45)	38 (27-58)



* p<0.05 compared with patients ≥ 65 years of age.

- *Pituitary Source*:

Pituitary Source			
	Young (≤45 years)	Middle-age (45-64 years)	Elderly (≥65 years)
Patients	48	27	6
Patient Characteristics			
Age , mean (median)	32.9 (35)	52.3 (53)	71.3 (71)
BMI, mean (median)	29.6 (29.7)	33.8 (34.3)	28.7 (24.3)
Biochemical Data			
UFC, xULN, median (IQR)	3.5 (2.2-5.0)*	3.8 (2.5-5.7)*	4.6 (3.2-7.3)
Cortisol post LDDST, nmol/L,median (IQR)	345 (143-596)	412 (136-558)	688 (423-708)
ACTH, xULN, median (IQR)	1.3 (0.9-2.2)*	1.4 (1.0-1.8)*	1.7 (1.5-2.0)
Imaging Data			
Adenoma Size, mm, median (IQR)	6 (5-10)	7 (4-13)	8 (6-9)



* p<0.05 compared with patients ≥ 65 years of age.

Conclusion

- Older patients with Cushing syndrome have distinct disease cause and presentation, as pituitary source is less common than adrenal adenoma.
- Adrenal Cushing syndrome among elderly women is associated with milder hypercortisoluria and is frequently diagnosed incidentally.
- Weight gain was prevalent in young women undergoing investigation for hypercortisolism, and uncommon in older women.