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BACKGROUND

- Acromegaly, caused by excessive growth hormone(GH) secretion that stimulates insulin-like growth factor (IGF)-I production predominantly from the liver, results in considerable comorbidities, declines in quality of life, and increased mortality.¹⁻⁴
- Real world data on treatment patterns and morbidity of acromegaly patients who attained biochemical control compared with those who did not are limited.

OBJECTIVE

- To examine the relationship between achieving biochemical control and comorbidities.

METHODS

Study Design and Setting

- Retrospective cohort study from acromegaly registry at the Pituitary Center at Cedars-Sinai Medical Center (CSMC-PC), which has been recruiting patients since 1985.

Ethics and Safety

- The CSMC-PC registry contains only observational data, and the study was approved by the CSMC-PC institutional review board.

Study Population and Study Cohorts

- The study was not limited to patients initially diagnosed or treated at CSMC-PC. Patients were entered in the registry if they had care for acromegaly at CSMC-PC at any time after 1985 and had given informed consent.

- Biochemical-control status cohorts based on patients' final IGF-I or GH value:

- Controlled:** IGF-I $\leq 100\%$ of upper limit of normal; or GH nadir $< 1.0 \mu\text{g/L}$ within 2 hours following OGTT; or random GH level $< 1 \mu\text{g/L}$; or mean integrated 24-hour GH $< 2.5 \mu\text{g/L}$.
- Uncontrolled:** GH and/or IGF above levels noted.
- Discordant:** 2 tests within 7 days, and only 1 met definition of "controlled."

Study Measures

- Baseline measures were determined in the period from first lab test to 6 months from that date.
- Prevalence of comorbidities was determined across the entire period of enrollment in the registry.
- The following treatment changes were excluded from analysis:
 - Medications used briefly prior to surgery;
 - Octreotide SA use ≤ 30 days before octreotide LAR or lanreotide.
- Combination treatment meant simultaneous multiple medication use for > 90 days.

Statistical Analysis

- All statistical analyses were performed using SAS[®] version 9.4 (SAS Institute, Cary, NC).

RESULTS

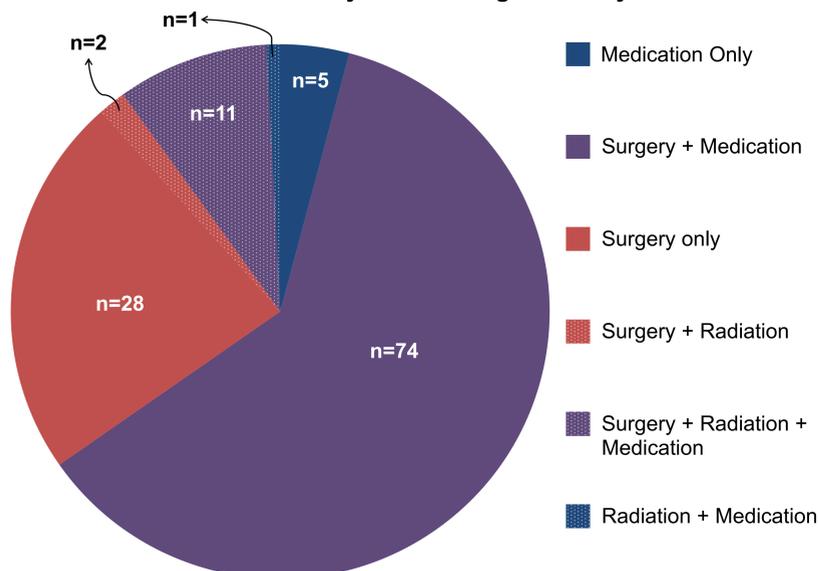
Baseline Characteristics

- 121 patients were followed for mean 8.8 years or 1065 patient years.
- Mean age was 55.4 years, and 55.4% were female.

Baseline Characteristic	Controlled N = 70; 57.9%	Discordant N = 16; 13.2%	Uncontrolled N = 35; 28.9%	All N = 121
Age, mean (SD)	55.0 (15.9)	52.6 (16.6)	57.6 (18.4)	55.4 (16.7)
Age at diagnosis, ^a mean (SD)	43.9 (14.7)	37.8 (14.4)	41.8 (15.8)	42.4 (15.0)
Female, n (%)	39 (55.7)	8 (50.0)	20 (57.1)	67 (55.4)
Race/ethnicity, n (%)				
Caucasian	51 (72.9)	11 (68.8)	26 (74.3)	88 (72.7)
Asian	8 (11.4)	0 (0.0)	8 (22.9)	16 (13.2)
Hispanic	9 (12.9)	3 (18.8)	0 (0.0)	12 (9.9)
Other	9 (12.9)	3 (18.8)	0 (0.0)	12 (9.9)
Macroadenoma (tumor size ≥ 1 cm), n (%)	59 (84.3)	9 (56.3)	25 (71.4)	93 (76.9)
Adrenal insufficiency, n (%)	10 (14.3)	3 (18.8)	5 (14.3)	18 (14.9)
Gonadal insufficiency, n (%)	16 (22.9)	0 (0.0)	4 (11.4)	20 (16.5)
Hypothyroidism, n (%)	10 (14.3)	2 (12.5)	7 (20.0)	19 (15.7)
Years of follow-up, ^b mean (SD)	8.5 (6.7)	10.9 (9.5)	8.5 (7.1)	8.8 (7.2)

^a 109 patients had information about age at diagnosis; ^b The period between the first and the last IGF-I/GH test date; Prolactin elevation was observed in 1 (6.3%) patient in the discordant group. But not all patients had data on prolactin elevation recorded at presentation at CSMC-PC because presentation may have occurred prior to care at CSMC-PC and prolactin elevation information was not available on all patients.

Treatment Received at Any Time During the Study Period



Treatment

- Treatment was initially surgery in 104 patients (86%), medication in 16 (13%), and radiation in 1 (1%).
- In 104 with initial surgery, 78 (75%) had further therapy: 7 had a second surgery, 67 had pharmacotherapy (48 had SRLs; 19 had dopamine agonists), and 4 radiation.
- In 16 on first-line pharmacotherapy, 13 (81%) received further treatment: 4 had surgery and 9 had further pharmacotherapy.
- By the end of follow-up, 88 (73%) patients required treatment with multiple modalities.

Clinical Outcomes

- Diabetes mellitus (DM), hypertension (HTN), sleep apnea, and cardiomyopathy were less frequent in controlled compared to uncontrolled patients.
- The prevalence of HTN, DM, and sleep apnea were higher in this registry than in European registries: 39.4%, 25.3%, and 17.1%, respectively, in the Belgian registry⁵; and 39.1%, 37.6%, and 13.2%, respectively, in the Spanish registry.⁶

Outcome, n (%)	Controlled N = 70; 57.9%	Discordant N = 16; 13.2%	Uncontrolled N = 35; 28.9%	All N = 121
Hypertension	30 (42.9)	7 (43.8)	21 (60.0)	58 (47.9)
Diabetes mellitus	18 (25.7)	5 (31.3)	15 (42.9)	38 (31.4)
Sleep apnea	17 (24.3)	1 (6.3)	10 (28.6)	28 (23.1)
Colonic polyps or colon cancer	15 (21.4)	1 (6.3)	8 (22.9)	24 (19.8)
Visual field defects	12 (17.1)	2 (12.5)	6 (17.1)	20 (16.5)
Left ventricular hypertrophy	9 (12.9)	0 (0.0)	4 (11.4)	13 (10.7)
Cardiomyopathy or heart failure	3 (4.3)	0 (0.0)	3 (8.6)	6 (5.0)

LIMITATIONS

- Many patients were initially treated elsewhere before referral to CSMC-PC. Results therefore reflect care from a variety of providers and may have been incompletely documented.
- Institutional variation may limit the generalizability of these findings.
- Small numbers make statistical comparisons not possible.

CONCLUSIONS

- This study confirms that biochemically uncontrolled patients with acromegaly appear to suffer from a greater number of common comorbidities than their controlled counterparts.
- Despite the use of multiple treatment modalities, almost a third of patients remain biochemically uncontrolled, demonstrating the difficulty of achieving biochemical control.

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