A Multi-Center Study of Follow-Up Intervals in Patients with Cushing's Disease

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BACKGROUND

- Cushing's disease (CD) has an annual incidence of 1.2-2.4 per million in Europe and up to 8 per million in the U.S.[1-3]
- Uncontrolled CD has significant morbidity and mortality.[4]
- Long-term follow-up of CD is essential to mitigate risks of increased morbidity/mortality.[5]
- No recommendations exist to guide follow up frequency, in part because the actual frequency with which CD patients are followed in clinical practice is unknown.

OBJECTIVE

- To determine the pattern and frequency of follow-up for CD patients in the US.

METHODS

Study Design and Data Source

- Retrospective data collected from medical records at 8 US pituitary/endocrine centers, selected based on volume of CD patients, location, and patient diversity.
- The study was approved by institutional IRBs.

Patient Selection

- Inclusion criteria:
  - Diagnosed with CD or CD recurrence within past 20 years; AND
  - ≥18 years old at diagnosis.

Data Collection

- Data collected from onset of CS symptoms through 2014
  - Demographics (age, sex, race/ethnicity),
  - Disease characteristics: onset of CS symptoms, date of diagnosis of CD, CD recurrence, biochemical status,
  - CD treatments delivered at study centers and local practices,
  - Comorbidities
    - Prevalence was based only on comorbidities reported at the study centers,
  - Final disposition: date of last visit, evidence of transfer of care, insurance status at last visit.
- Data quality measures included rigorous abstractor training, data quality checks, and follow-up abstraction for inconsistencies and missing entries.

Statistical Analysis

- Results stratified by length of time since last visit.
- Descriptive statistics, including mean, median, standard deviation, and percentage, were reported.
- Data transformations and analyses performed with SAS® version 9.4 (SAS Institute, Cary, NC).

RESULTS

Patient and Follow-Up Characteristics

- By 1/15/15, data regarding 163 patients had been entered in the database, and formed the basis of this analysis.
- 90 patients (55%) were last seen within 1 year, 32 (20%) within 1-2 years, and 41 (25%) >2 years prior (Table 1).
- Recurrent or residual disease was more commonly observed for those seen 1-2 years or >2 years prior (Table 1).
- Evidence of transfer of care, with presumed follow up elsewhere, was noted in 4%, 13% and 37% with last visit ≤1, 1-2, and >2 years prior, respectively (Table 1).

Table 1. Patient Characteristics, by Follow-Up Interval

Characteristic	Time since last visit ≤1 year	1-2 years	>2 years
N	90	32	41
Age at last visit (years), mean ± SD	47 ± 13	44 ± 15	44 ± 14
Median [range]	47 [23-83]	43 [21-73]	42 [19-79]
Female, n (%)	65 (72)	25 (78)	39 (95)
Race, Caucasian, n (%)[a]	65 (89)	20 (95)	26 (81)
Black	7 (10)	0 (0)	3 (10)
Other	1 (1)	1 (5)	3 (10)
Ethnicity, Hispanic/Latino, n (%)	13 (14)	4 (13)	7 (17)
No. of comorbidities, mean ± SD[b]	3. 9 ± 2.5	2.3 ± 1.6	3.1 ± 2.1
Insurance status	84 (93)	31 (97)	38 (93)
Insured, n (%)			
Uninsured, n (%)	6 (7)	1 (3)	3 (7)
Recurrent/residual disease, n (%)	47 (52)	23 (72)	29 (71)
Time from diagnosis to last visit (years), median [range]	3.8 [0-27.4]	2.8 [0-18.8]	1.6 [0-21.7]
Follow-up duration at study centers[c] (years), median [range]	2.3 [1-27.5]	1.2 [1-6.4]	1.1 [1-21.7]
Documented transfer of care, n (%)	4 (4)	4 (13)	15 (37)

[a] percent among non-missing observations
[b] based on comorbidities reported at study centers
[c] from first to last visit

Treatment for Cushing's Disease

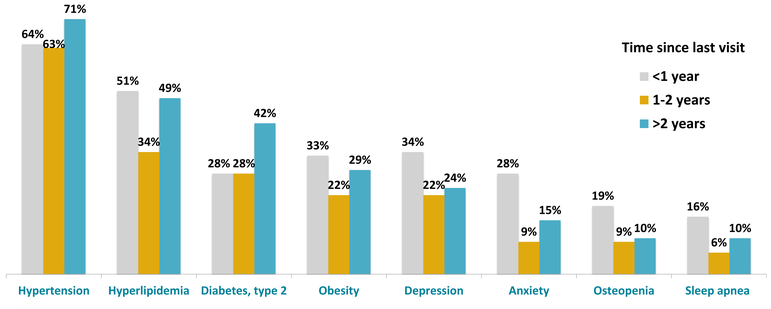
- 96% underwent surgical removal of pituitary adenoma as first-line therapy.
- Among 64 patients with residual/recurrent CD, 36 (56%) received pharmacotherapy, 20 (31%) underwent radiation therapy, and 9 (14%) were treated with adrenalectomy.
  - Fewer patients with last visit >2 years prior had radiotherapy (8%) compared to those seen within 1 year (42%) (Table 2).
- Median elapsed time from start of most recent type of therapy to last visit was shorter among patients last seen >2 years prior compared to those seen within 1 year, 4.7 vs. 11.6 months, respectively.

Table 2. Treatment for Recurrent/Residual CD[a]

Patients with recurrent/residual CD	Time since last visit ≤1 year	1-2 years	>2 years
No. of patients	N=43	N=9	N=12
Pharmacotherapy	27 (63)[b]	2 (22)	7 (58)
Radiotherapy	18 (42)	1 (11)	1 (8)
Adrenalectomy	7 (16)	0 (0)	2 (17)

[a] any therapies from first documented date of residual/recurrent CD to last visit at study site
[b] n (%)

Figure. Prevalence of Individual Comorbidities, by Follow-Up Interval



LIMITATIONS

- Data on care outside the study center was likely underreported in medical records at study sites.
- These results are interim descriptive analyses. At study completion, statistical analyses will be conducted.
- Care and follow-up patterns at the 8 study centers may not be representative of all US centers.

CONCLUSIONS

- Many patients with CD went more than 1 year without a visit and a majority of these patients did not have documented transfer of care, but it is possible that some are being followed elsewhere.
- A higher proportion of patients seen >1 year had evidence of recurrent/residual disease.
- Patients not seen for extended periods may be at risk of undiagnosed recurrence or progression of CD and development of comorbidities, unless they are being seen at other centers.
- Further investigation of factors that increase the risk of becoming lost to follow-up warrant closer examination in order to prevent or mitigate undetected recurrence or progression of CD.

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