ACROPOLIS study: differences in symptoms and comorbidities in 472 patients with acromegaly according to the sex of patients and sources of clinical data

Philippe Caron,[1] Thierry Brue,[2] Gérald Raverot,[3] Antoine Tabarin,[4] Anne Cailleux,[5] Brigitte Delemer,[6] Peggy Pierre Renoult,[7] Aude Houchard,[8] Benedicte Duclos-Morlaes,[8] Philippe Chanson[9]

[1]Hôpital Larrey, Toulouse; [2]Hôpital de la Timone, Marseille; [3]Groupement Hospitalier Est, Lyon; [4]Hôpital Haut-Lévêque, Pessac; [5]CHU Rouen–Hôpital de Bois Guillaume, Bois Guillaume; [6]CHU Reims – Hôpital Robert Debré, Reims; [7]CHU Bretonneau, Tours; [8]Ipsen Pharma, Boulogne-Billancourt; [9]CHU Bicêtre, Le Kremlin Bicêtre, France

Introduction

- Aromegaly is a rare, long-term, multisystem disease characterized by excessive growth hormone (GH) secretion and elevated insulin-like growth factor-1 (IGF-1), and caused by a benign pituitary adenoma.[1]
- A broad range of signs/symptoms and comorbidities are caused by the tumour itself and by the long-term effects of GH/IGF-1 on multiple organs and tissues.[1,2]
- Diagnosis is often delayed, by up to a decade in some patients.[2] This reflects the non-specific nature of many of the signs/symptoms and comorbidities, the insidious onset of differentiating features and lack of disease awareness amongst healthcare professionals.[3]
- As early diagnosis may increase the rate of successful treatment[4] and is important for preventing long-term comorbidity and premature death,[5] improved awareness of the signs/symptoms and comorbidities of acromegaly is key.

Objective

- The ACROPOLIS study was designed to characterize the signs/symptoms and comorbidities of acromegaly at diagnosis in a large cohort of patients.

Methods

- Non-interventional observational cross-sectional multicentre study conducted in France between 2013 and 2014.
- Adults with acromegaly diagnosed <5 years previously were included.
- Data were collected from two sources: retrospectively from patients' medical records (transcribed into case report forms [CRFs]), and patients were also asked to complete self-administered questionnaires. Demographic and disease characteristics were captured, including the signs/symptoms and comorbidities of acromegaly and dates of occurrence.
  - A *post-hoc* analysis was conducted to evaluate the evolution of manifestations prior to diagnosis.
  - Differences in the reporting of manifestations according to data source were described using a rate of discrepancy (percentage of patients reporting a manifestation in either the patient's questionnaire or the patient's medical records, but not both).

Results

Patient characteristics at diagnosis of acromegaly

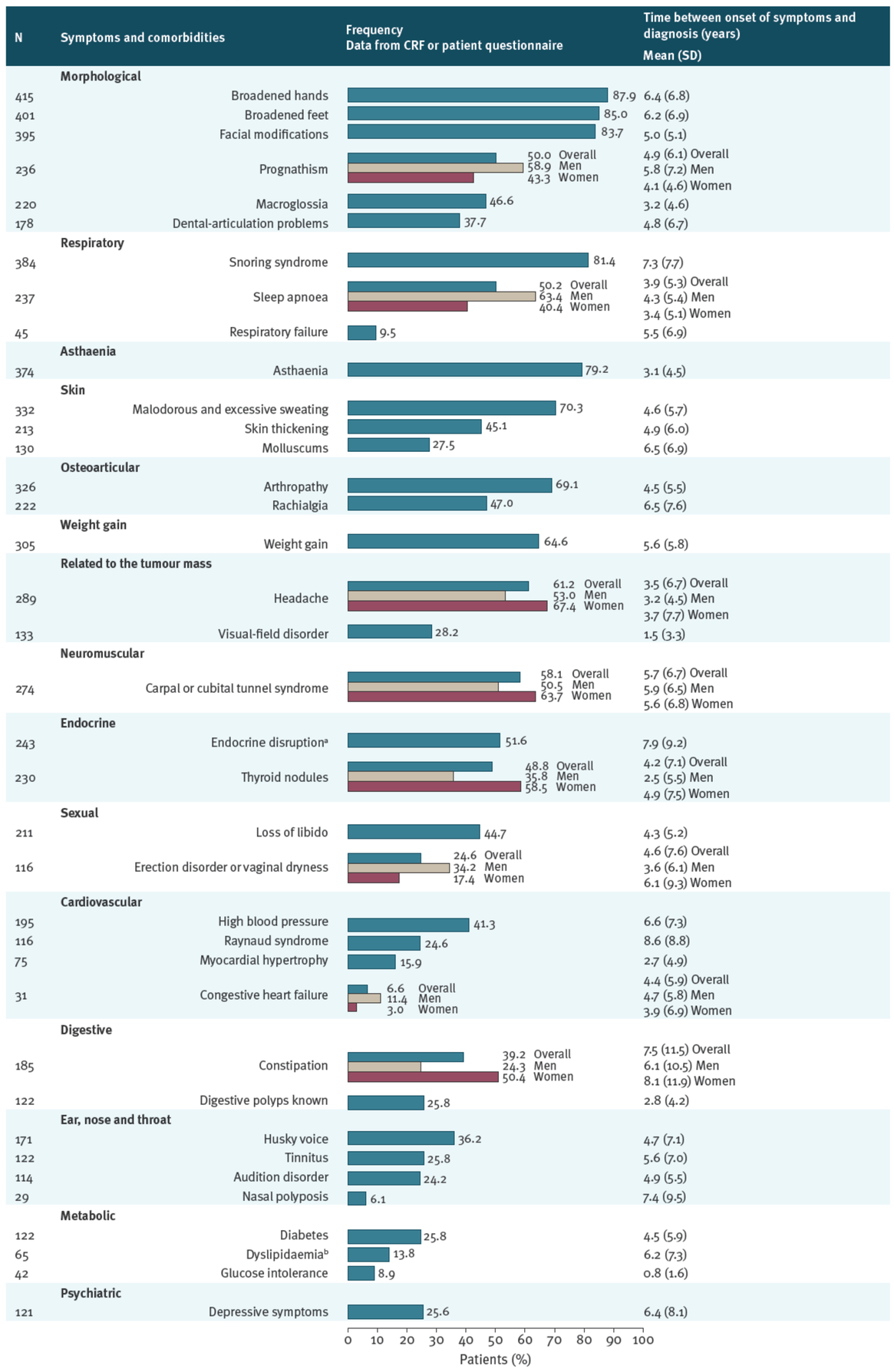
- In total, 648 patients were enrolled in the study; of these, 472 met the inclusion criterion, had both a completed CRF and a completed patient questionnaire, and were therefore included in the analysis.
- Patient demographic and disease characteristics are summarized in **Table 1**.

Table 1. Patient demographic and clinical characteristics at diagnosis of acromegaly

	Study population (N=472)
Age (years)	51.9 (±14.3)
BMI (kg/m²)	n=436 27.7 (±5.3)
Sex, n (%) Men Women	202 (42.8) 270 (57.2)
Time since diagnosis (months)	30.6 (±17.8)
Acromegaly diagnosed by, n (%): Endocrinologist General practitioner[a] Others[b]	n=427 126 (29.5) 69 (16.1) 232 (54.3)
Type of pituitary adenoma GH GH/prolactin Other	n=462 364 (78.8) 84 (18.2) 14 (3.0)
Tumour size Microadenoma (<10 mm) Macroadenoma (>10 mm)	n=456 89 (19.5) 367 (80.5)
GH (ng/mL) ≤2.5 >2.5	n=277 48 (17.3) 229 (82.7)
IGF-1 (% ULN)	n=406 295 (±160)
Serum prolactin[c] (ng/mL)	n=62 183 (±650)

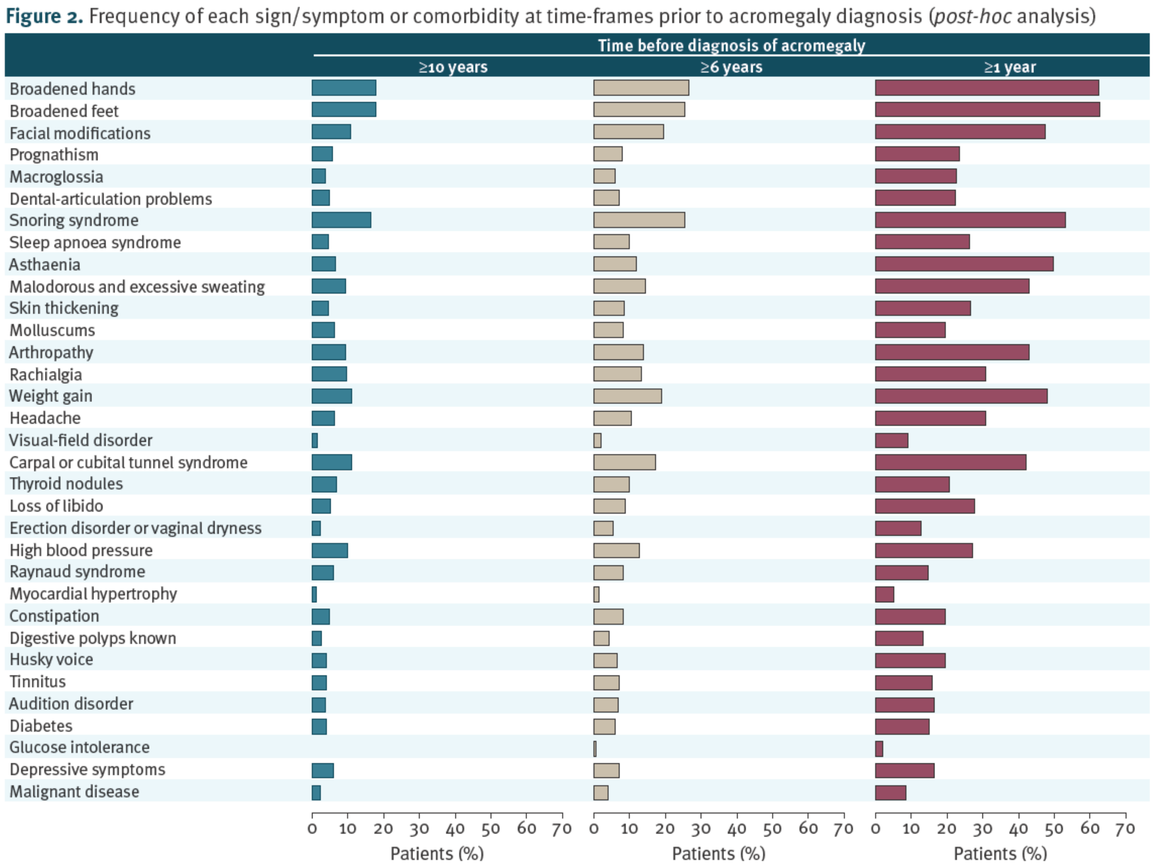
Data are mean (±SD) unless stated otherwise. [a]General practitioner (13.8%) and substitute for general practitioner (2.3%); [b]other specialists (37.2%) and other (healthcare professional/patient/patients' relatives, 17.1%); [c]for GH/prolactin adenomas. BMI, body mass index; GH, growth hormone; IGF-1, insulin-like growth factor-1; ULN, upper limit of normal.

Figure 1. Frequency of signs/symptoms and comorbidities and time to acromegaly diagnosis in the overall study population (and according to sex for those signs/symptoms and comorbidities with sex differences)



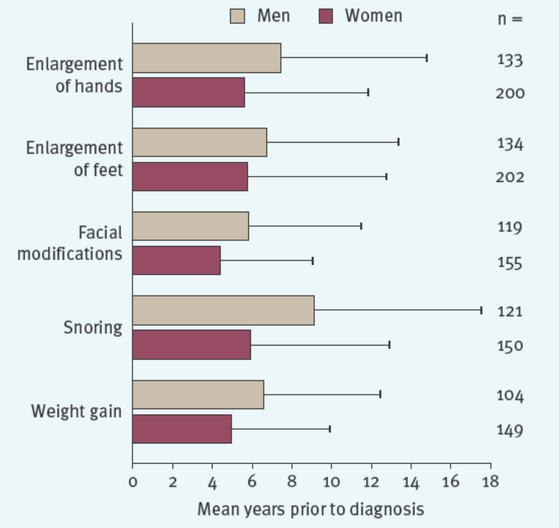
[a]Amenorrhoea or spaniomenorrhoea, hair growth increase and/or acne in women; gynaecomastia in men; [b]Reassignment.

Figure 2. Frequency of each sign/symptom or comorbidity at time-frames prior to acromegaly diagnosis (*post-hoc* analysis)



Signs/symptoms and comorbidities prelisted in the CRF and in the patient questionnaire that were reported by patients are described at time-frames before the diagnosis of acromegaly. Results are presented for the overall patient population, n=472.

Figure 3. Mean time between the detection of early acromegaly manifestations (morphological modifications, snoring and weight gain) and diagnosis in men and women



Error bars represent standard deviation.

Frequency of signs/symptoms and comorbidities at diagnosis

- At diagnosis, patients presented a broad range of signs/symptoms and comorbidities.
  - The incidence of a number of manifestations tended to differ between the sexes: headache, carpal/cubital tunnel syndrome, constipation and thyroid nodules were more common in women, while prognathism, sleep apnoea syndrome and congestive heart failure were more common in men (**Figure 1**).

Evolution of signs/symptoms and comorbidities prior to diagnosis (post-hoc analysis)

- Mean (standard deviation, SD) time between onset of manifestations and acromegaly diagnosis was 5.1 (± 6.8) years.
- The mean (SD) time between the earliest manifestation and acromegaly diagnosis was 14.2 (± 11.3) years.
- The evolution of manifestations in the years prior to diagnosis is summarized in **Figure 2**.
  - The earliest manifestations were morphological (enlargement of extremities, changes in facial features), snoring and weight gain. Morphological manifestations, snoring and weight gain tended to be detected earlier in men than in women (**Figure 3**).

Differences in signs/symptoms and comorbidities according to data source

- There were differences in the reporting of manifestation between the patients' questionnaires and patients' medical records (CRFs).
- Of the 39 manifestations reported, rates of discrepancy ranged from 5.5% to 36.2%.
  - Of these, manifestations reported at highest rates of discrepancy were: snoring (36.2% [171/472]), weight gain (35.8% [169/472]), loss of libido (34.5% [163/472]), rachialgia (33.5% [158/472]), asthaenia (33.5% [158/472]), and arthropathy (32.6 [154/472]).

Conclusions

- The ACROPOLIS study confirms the broad range of acromegaly manifestations at diagnosis.
- Key manifestations detected earliest, prior to diagnosis, were morphological modifications, snoring and weight gain, which evolved slowly over many years.
- Sex differences were observed in terms of the frequency of manifestations and time between onset and diagnosis.
- Differences in the reporting of manifestations between patient and clinician were most evident for snoring, weight gain, loss of libido, asthaenia, rachialgia, and arthropathy.

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