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The impact of adjustments to the diagnostic criteria for biochemical remission in surgically treated patients with acromegaly

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ABSTRACT

Background: The suggested criteria for biochemical remission in patients treated for acromegaly were recently modified. The aim of this project was to study to what extent this modification influences remission rates.
Design, patients and methods: This was a retrospective study of 55 consecutive patients [29 men; median age 47 years (interquartile range 38–68)] diagnosed with acromegaly between 2003 and 2014. After treatment serum IGF-I and/or GH was measured according to a standardized protocol. The biochemical remission status was defined according to the clinical guidelines from 2010 and2014.
Results: Out of 55 patients, 44 patients were primarily operated. Of these, 33 (75%) were evaluated 3–12 months postoperatively by measuring serum IGF-I and GH during an oral glucose tolerance test. According to the 2010 guidelines, 11 patients (33%) were in biochemical remission, 15 patients (46%) were not and 7 patients (21%) had discordant results (normal IGF-I and high GH or vice versa). Applying the 2014 guidelines in the same group, 16 patients (49%) were in biochemical remission, 7 patients (21%) were not and 10 patients (30%) had discordant results. Thus, by using the most recent criteria for biochemical control, more patients were considered to be in remission, or with discordant results, and fewer patients not in remission ($P < 0.05$).
Conclusion: An apparently minor adjustment of the criteria for biochemical control has a significant impact on remission status in patients treated for acromegaly, eventually affecting follow-up and treatment strategies.

1. Introduction

Acromegaly is a rare disease caused by a persistent hypersecretion of growth hormone (GH), almost always due to a pituitary adenoma [1]. GH stimulates the secretion of insulin-like growth factor I (IGF-I) from the liver, which together with GH, causes the majority of the clinical manifestations of acromegaly [1]. Comorbidities are prevalent and mortality is high, especially if biochemical control is not achieved [1–8].

The definitions of “biochemically controlled disease” and “cure” have changed over the years regarding treated acromegaly [9–11]. The development of more sensitive and specific assays for measurement of GH and IGF-I have resulted in different cut-off values for remission [2,3,10]. Taking this into account, the Endocrine Society has recently updated it's guidelines for the evaluation and management of acromegaly [11,12]. In 2010, biochemical remission was defined as a normal age-adjusted IGF-I along with suppressed GH < 0.4 μg/L [10]. In 2014 the level for suppressed GH was raised to < 1.0 μg/L [11]. To which extent this modification affects the assessment of remission status in patients with acromegaly is poorly studied.

The aim of this study was to evaluate the impact of the different proposed criteria, as well as the impact of two different IGF-I assays, on the biochemical remission status in patients treated for acromegaly. Our hypothesis was that both the modification of the diagnostic criteria and the use of a new IGF-I assay have a significant effect on remission status.

2. Design, material and methods

2.1. Study design and patients

This was a retrospective study of 60 consecutive patients diagnosed with acromegaly between 2003 and 2014 at the Sahlgrenska University Hospital in Gothenburg, Sweden. Patients who had received the ICD-10

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code for acromegaly (E22.0) were identified through search in the electronic medical records at our hospital. Clinical, biochemical, radiological and histopathological data at diagnosis were reviewed in all patients. Furthermore, clinical and biochemical data 3–12 months postoperatively and at the last clinical visit were collected. Biochemical data before and after the IGF-I method was changed at our hospital from Immulite 2500 to IDS-iSYS (April 2013) were also collected.

In total, 60 patients fulfilling the search criteria were identified. Of these, five patients were excluded; two did not have acromegaly, one was neither operated nor followed-up at our hospital, one was lost to follow-up and one had rapidly growing, treatment resistant, GH producing atypical pituitary adenoma. Thus, 55 patients with acromegaly were included in this analysis.

2.2. Follow-up protocol

Patients that were operated for acromegaly, except for patients clearly not in remission directly after the surgery (based on known residual tumor and considerably elevated IGF-I/GH; n = 8), were evaluated clinically and biochemically 3–12 months postoperatively (n = 36) by measuring IGF-I (n = 36) and GH following an oral glucose tolerance test (OGTT; 75 g glucose; n = 33; Fig. 1). Patients who were not in remission received either additional treatment (reoperation, radiotherapy or medical treatment) or, were subjected to re-evaluation 3–6 months later (patients with mildly elevated GH and/or IGF-I). Thereafter, all patients were followed regularly both clinically and by measuring IGF-I every 6–12 months. Patients who had primarily received medical treatment (i.e., not operated) were initially followed every sixth week and after biochemical control had been achieved every 6–12 months.

2.3. Definitions of biochemical remission

Biochemical remission status was evaluated by using both the Endocrine society's clinical practice guidelines from 2010 [11], as well as the most recent guidelines from 2014 [10]. According to the guidelines from 2010 patients with IGF-I in the normal range (age- and sex-adjusted) and GH < 0.4 μg/L following an OGTT were considered to be in remission. According to the guidelines from 2014, biochemical remission is defined as normal IGF-I (age- and sex-adjusted) and a serum GH < 1.0 μg/L, collected either randomly or following OGTT.

2.4. Assays

Between 2003 and September 2006, IGF-I was measured by using a chemiluminescence immunoassay (Nichols Advantage; Nichols Institute

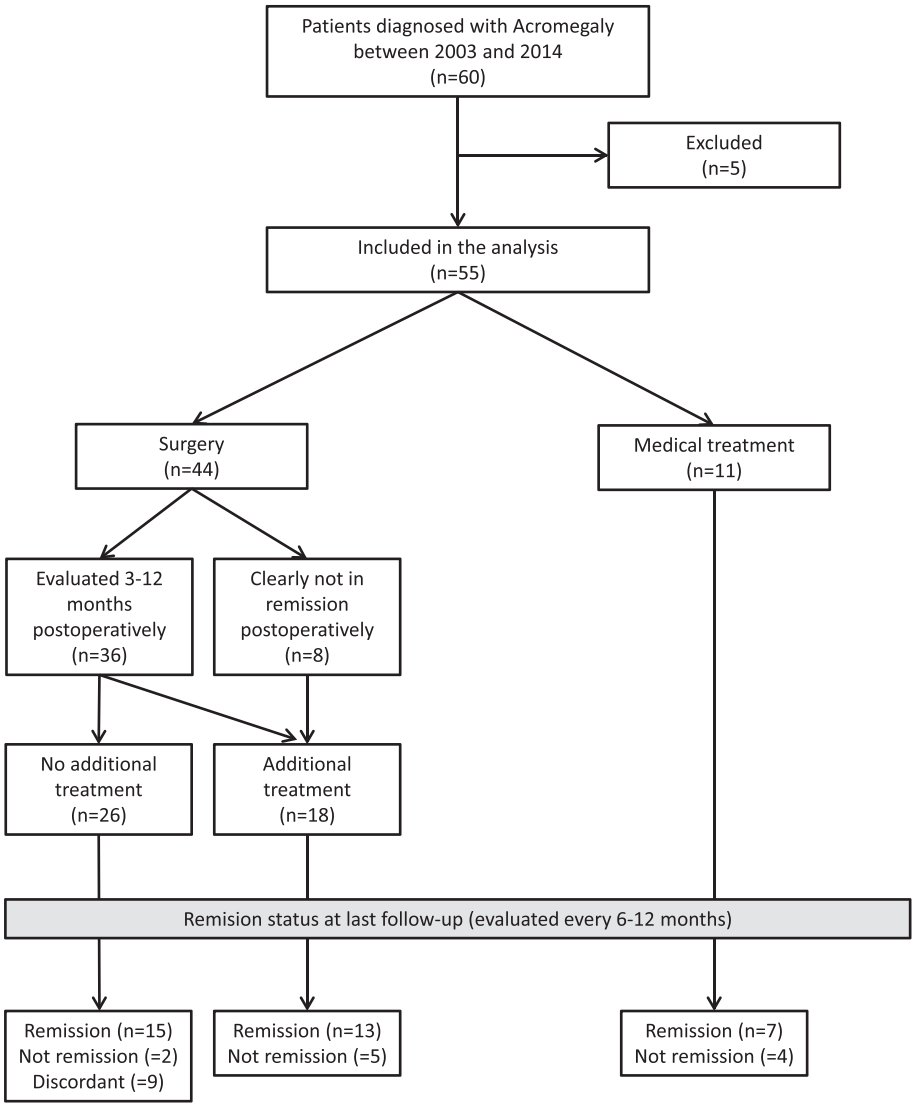

Fig. 1. The study population.