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Comparison of Various Therapeutic Options in the Treatment of Acromegaly - Analysis of the German Acromegaly Register

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for the Participants of the German Acromegaly Register

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DEUTSCHES AKROMEGALIE REGISTER

Introduction:

Medical therapy with somatostatin analogues (SSA) has been discussed as an alternative to surgery in patients with acromegaly. We analyzed the newly established German Acromegaly Register for the various treatment options used during the treatment of acromegaly. The German Acromegaly Register is an initiative of the Pituitary Working Group of the German Endocrine Society. The aim of the German Acromegaly Register is to collect data on patients suffering from acromegaly in Germany, both retrospectively and prospectively.

Methods:

The Register uses the UK electronic database to assure comparison between these two countries with different health care systems. All German health care providers are invited to participate. To assure correct and uniform data entry, two trained nurses visit all centers for data acquisition. GH and IGF-1 levels are those reported by case notes. Due to variations in assays and reference ranges, normalization of IGF-1 is assessed using local criteria. Sponsorship is provided by an unrestricted grant from Novartis Oncology, Germany.

Results are expressed as median (range), graphs demonstrate the median and interquartile range. GraphPad Prism 4.0 (GraphPad Software Inc., San Diego, USA) was used for statistical analyses, applying the Mann Whitney test.

Results:

At the time of this analysis, retrospective data from 1543 patients had been entered into the database (Fig.1), with a median age at diagnosis of 44 (6-86) years. Initial random GH levels of patients with biochemical data available were 15.9 (0.1-620.0) ng/ml, with 93.8% of GH levels >2.5 ng/ml and 95.3% of IGF-1 levels elevated. Radiological evaluation revealed micro- and macroadenomas in 21.2% and 78.8% of patients, respectively.

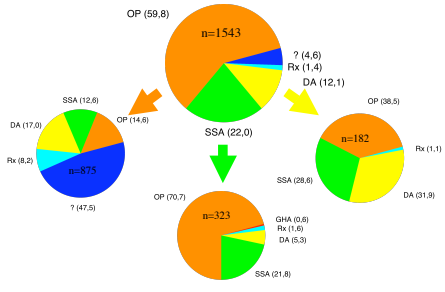

Fig.1 Primary (large circle) and secondary (small circles) treatment of patients with acromegaly, as determined by analysis of the German Acromegaly Register

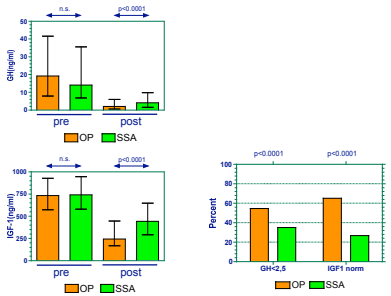

Fig.2 Pre- and post-treatment GH (upper left) and IGF1 (lower left) levels, and control rates of GH and IGF1 (right) after primary surgery (OP) or primary SSA (SSA)

Three hundred twenty one patients received at least 1 mo of SSA as primary therapy, with biochemical data available for re-evaluation in 211 patients treated for 5.1 (1-143) mo (Fig.2). GH<2.5 ng/ml were found in 35.1% of patients, and normal IGF-1 in 26.7%.

Secondary treatment included surgery (70.7%), dopamine agonists (5.3%), growth hormone antagonist (0.6%), and radiotherapy (1.6%) (Fig.1).

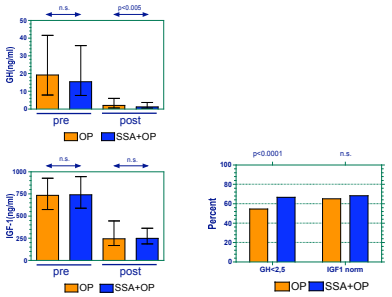

Fig.3 Pre- and post-treatment GH (upper left) and IGF1 (lower left) levels, and control rates of GH and IGF1 (right) after primary surgery (OP) or surgery with preoperative SSA (SSA+OP)

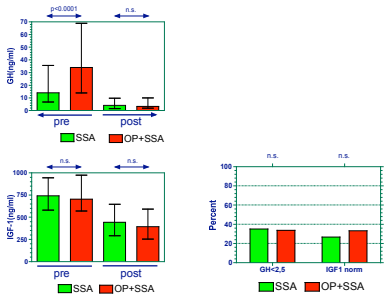

Fig.4 Pre- and post-treatment GH (upper left) and IGF1 (lower left) levels, and control rates of GH and IGF1 (right) after primary SSA or SSA after debulking surgery (OP+SSA)

In contrast, 923 patients were primarily treated by surgery, with biochemical data without concomitant treatment available for 571 patients (pre-therapy biochemical data n.s. to primary SSA, Fig.2). GH<2.5 ng/ml were found in 54.6% of patients (p<0.0001 to SSA), and normal IGF-1 in 65.2% (p<0.0001 to SSA).

Secondary treatment (Fig.1) included 2nd surgery (14.6%), SSA (12.6%), dopamine agonists (17.0%), and radiotherapy (8.2%).

In 135 patients treated with SSA prior to surgery and biochemical data available (SSA+OP, pre-operative biochemical data n.s. to OP, Fig.3), postoperative evaluation revealed GH<2.5 ng/ml in 66.7% of patients (p<0.05 to OP), and normal IGF-1 in 68.3% (n.s. to OP).

In 75 patients treated by primary surgery followed by SSA (OP+SSA), pre-operative GH levels were significantly higher than in primary SSA (p<0.0001, Fig.4). GH levels after treatment were not significantly different. However, GH% of initial GH was significantly lower in secondary compared to primary SSA (41.1+/-17.0 vs. 71.7+/-11.1, p<0.005, not shown). IGF-1 levels were similarly affected in both groups.

Summary:

- Primary medical treatment with SSA allowed for biochemical control in a relevant number of patients, with primary surgery demonstrating higher biochemical success rates.
- Efficacy of SSA may have been limited by the preparations and doses used, and the duration of treatment in this retrospective evaluation.
- Pre-operative therapy with SSA may improve the biochemical outcome.
- On the other hand, debulking surgery may improve the biochemical response rates of SSA therapy.
- Prospective studies are necessary to compare these various treatment options in more detail.

Participants of the German Acromegaly Register:

Biering H, Blossey HC, Blum H, Bogner U, Buchfelder M, Caspar-Bell G, Demtröder F, Diederich S, Droste M, Faust M, Finke R, Gräf KJ, Gerbert B, Grußendorf M, Hampel R, Heckmann C, Hehrmann R, Herrmann BL, Höffken K, Hüfner M, Jacobeit J, Jaursch-Hancke C, Jockenhövel F, Knippert A, Koch C, Kornely E, Krone W, Lehnert H, Levasseur S, Lößner C, Mann K, Meuser J, Meyer A, Minnemann T, Mönig HI, Müller UA, Paschke R, Petersenn S, Pfeiffer A, Plöckinger U, Raue F, Reincke M, Reschke K, Rudorff KH, Rühle H, Schopohl J, Schories M, Schröder H, Schröder HE, Schröder U, Schulte HM, Stamm B, Steinmetz M, Strasburger CJ, Tharandt L, Tuschy U, von Werder K, Weber MM, Würl K