Evidence for better response to somatostatin analogue treatment in acromegalic patients treated with metformin

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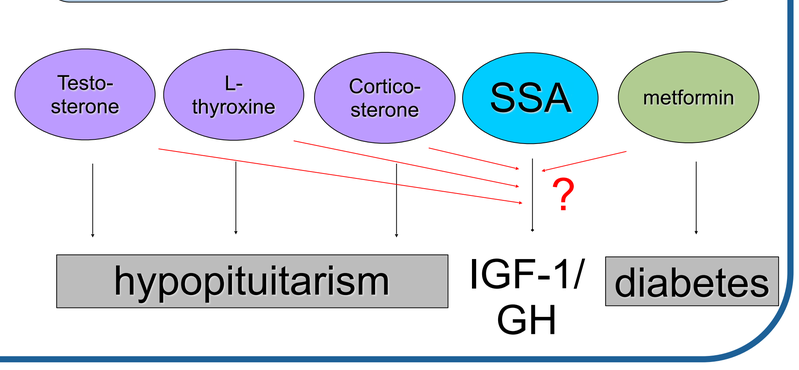
1 Backround

GH-secreting (Acromegaly)
- **Surgery: 60% cure**
- **Medical therapy (somatostatin analogs):**
  - **40-50% cure**
  - **40% resistance**
  - **SA+DA**
  - **GHR antagonist**
  - **repeat surgery/radiotherapy**

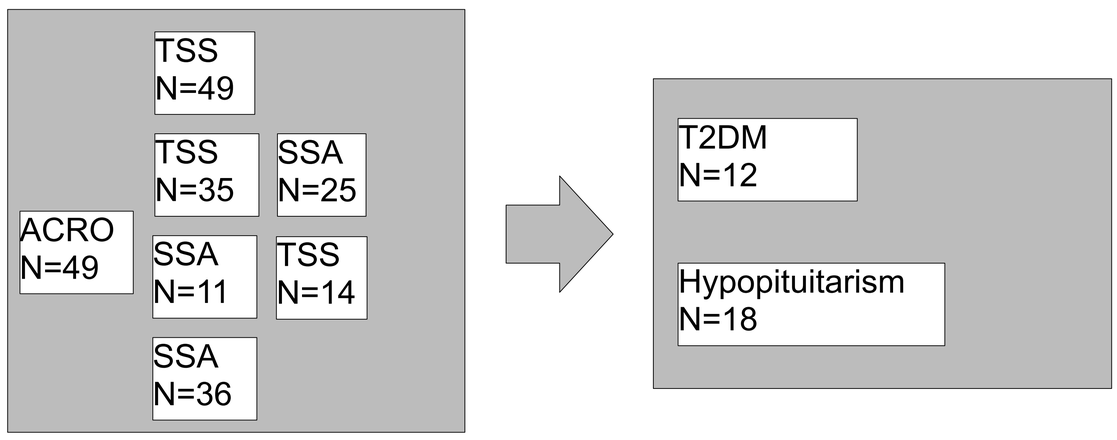
Comorbidities:

- Cardiomyopathy
- Hypertension
- Coronary artery disease
- **Hypopituitarism**
- **Diabetes mellitus**

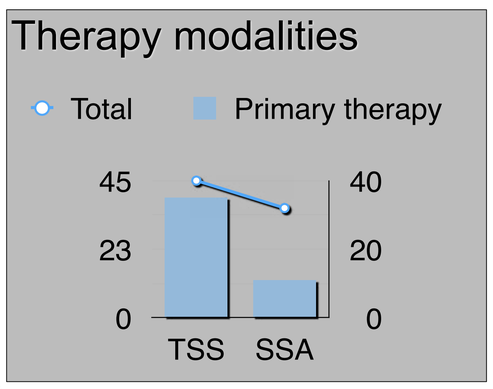
What is the impact of concomitant management of comorbidities to the response to somatostatin analog treatment



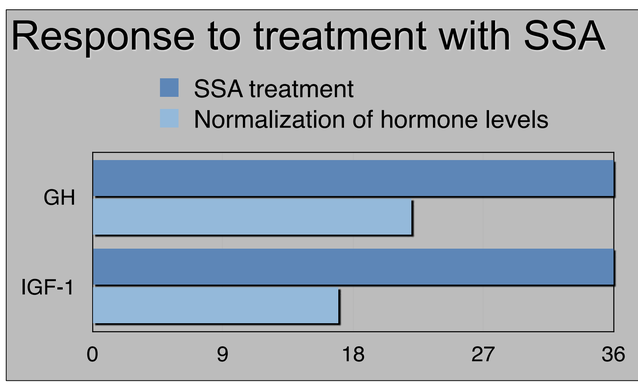
2 Cohort presentation



Therapy modalities



Response to treatment with SSA

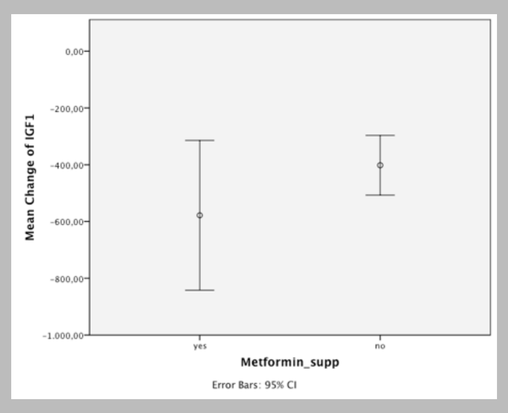


3 Metformin treatment correlates with improved response to SSA treatment

No correlation between age, gender, disease duration, other treatment modalities and change of IGF-1 after SSA treatment:

- Age p=0,183
- Gender p=0,397
- Disease duration p=0,686
- Hydrocortico-sterone p=0,173
- Testosterone p=0,085
- L-thyroxine p=0,721

Correlation between Metformin therapy and IGF-1 levels after SSA treatment

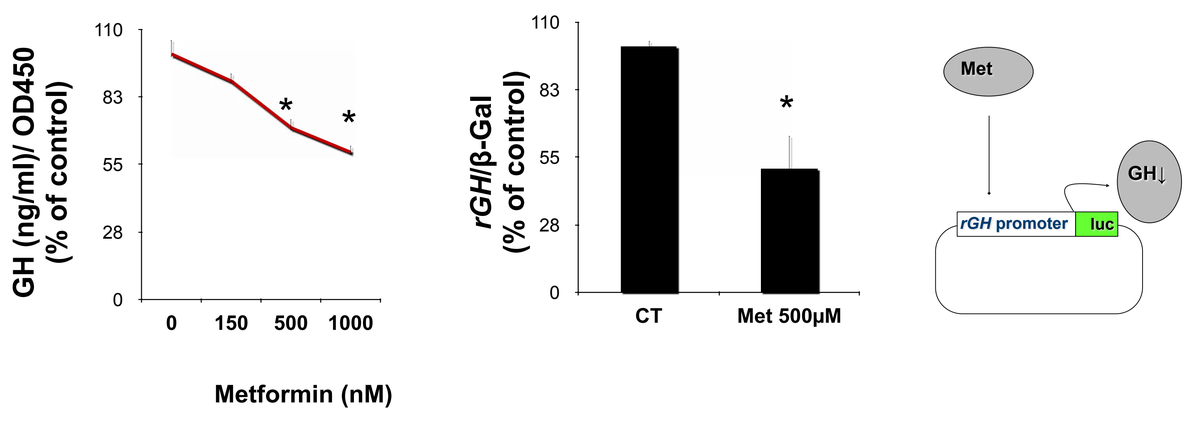


p=0,031; R-square change: 0,135; R-square: 0,321

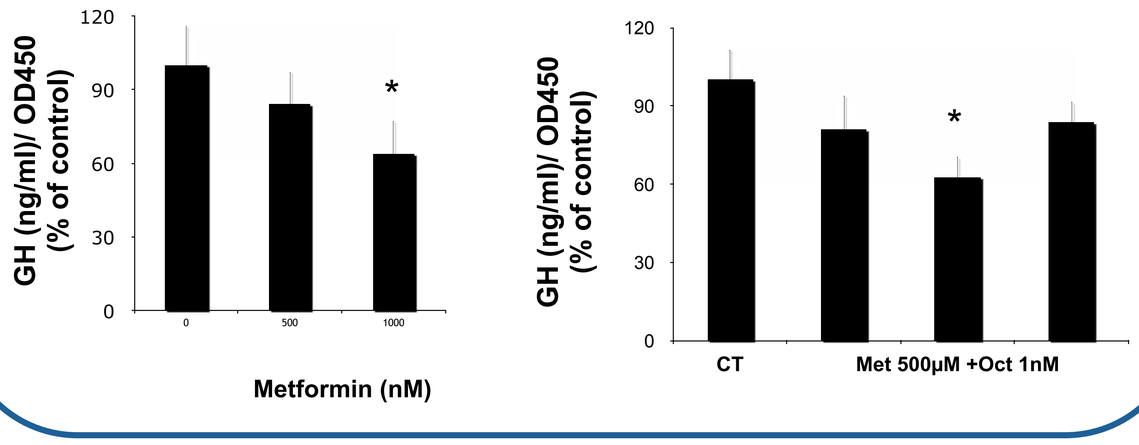
No correlation between IGF-1 lowering response to SSA and substitution treatment with hydrocorticosterone, testosterone, l-thyroxin (variance inflation factor <3)

4 Metformin reduces GH synthesis *in vitro*

In vitro experiments in GH3 cells



Human acromegalic tumors in vitro (n=7)



5 Summary

- The aim of this study was to analyze the impact of the concomitant antidiabetic treatment with metformin and hormone replacement on the response to SSA
- Data showed no correlation between SSA (p=0.71) and transsphenoidal surgery (p=0.541) on the incidence of pituitary insufficiency
- Regression analysis showed no correlation between IGF-1 lowering response to SSA and substitution treatment with hydrocorticosterone, testosterone, l-thyroxin (VIF <3)
- No correlation between age, gender, disease duration, other treatment modalities and change of IGF-1 after SSA treatment
- Linear regression analysis showed correlation between metformin therapy and change of IGF-1 levels after SSA treatment (p=0.031; R-square change: 0,135; R-square: 0,321)
- *In vitro* investigation showed that metformin enhances GH-suppressive effect of octreotide
- These preliminary observations indicate that hormone replacement does not affect SSA response, but metformin treatment improves SSA response in terms of IGF-1 reduction

ECE 2016 860-EP
Pituitary Basic
Moritz Winkelmann
Poster presented at: ECE2016 28 – 31 May 2016 MUNICH, GERMANY
PosterSessionOnline.com