The diagnostic value of serum IGF-II in combination with IGF-I and IGFBP-3 in Silver-Russell syndrome

Gerhard Binder[1], Thomas Eggermann[2], Karin Weber[1], Roland Schweizer[1]
[1]University Children's Hospital, Pediatric Endocrinology, Tuebingen, Germany
[2]Institute of Human Genetics, RWTH Aachen, Aachen, Germany

Introduction

Recently we described a multigenerational family with severe intrauterine and postnatal growth failure as well as signs of Silver-Russell syndrome (SRS) who carried a heterozygote nonsense mutation of *IGF2* (1). The patients had low IGF-II serum levels, but normal IGF-I levels.

Here, we aimed to estimate **the diagnostic value of IGF-II in combination with IGF-I and IGFBP-3 in the assessment of children with SRS**.

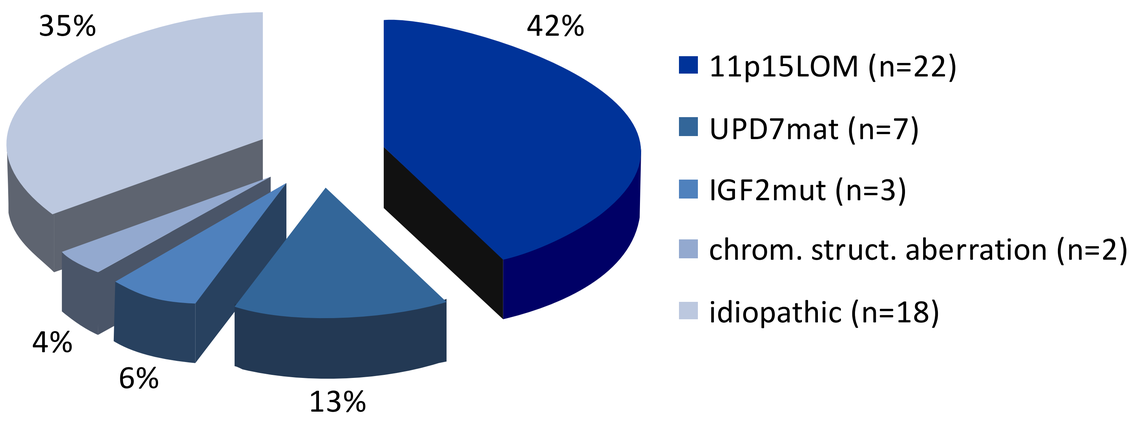
Individuals

We collected the data from 52 children with SRS (23 girls) with complete genetic and endocrine analysis, and 113 children with non-syndromic SGA short stature, seen during the last 20 years at our centre. The SRS children were 4.7 ± 2.1 y of age. A cohort of 113 SGA children aged 5.7 ± 1.8 y served as comparison. All patients were prepubertal and GH treatment naive when tested.

Table 1 The SRS patients fulfilled at least 4 of the following 6 criteria (NH-score):

- SGA at birth
- failure to thrive in infancy or BMI < -2 SDS
- short stature
- relative macrocephaly
- prominent forehead
- body asymmetry

Figure 1 Molecular genetics of the SRS group (n=52)

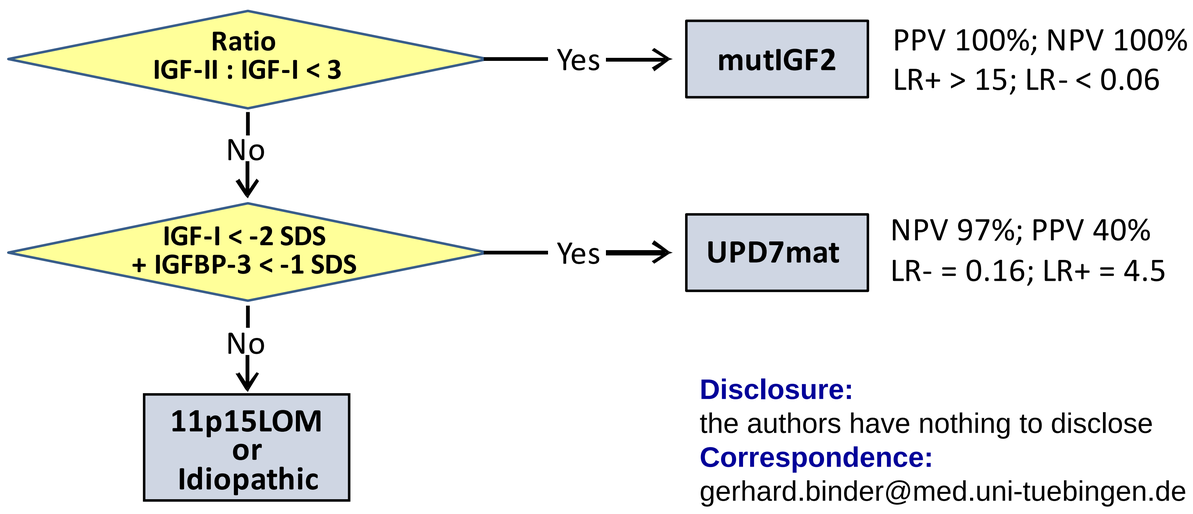


Methods

IGF-II, IGF-I and IGFBP-3 were measured by the same in-house RIAs during the full study period (2-3). Hormone SDS values are based on a reference cohort of healthy German and Danish children.

Conclusions

The molecular diagnosis in SRS can be predicted by measuring serum IGF-II in combination with IGF-I and IGFBP-3 as well as by calculating the IGF-II to IGF-I concentration ratio. The flow chart illustrates the predictive power of this approach:



Disclosure:
the authors have nothing to disclose
Correspondence:
gerhard.binder@med.uni-tuebingen.de

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Results

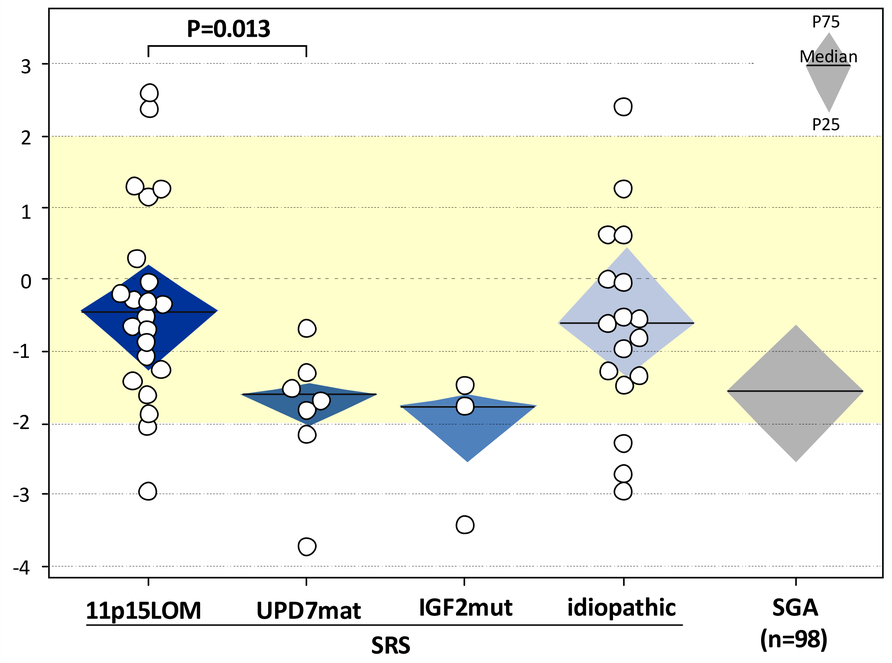

Figure 2

IGF-II SD scores: median, quartiles and individual scores.

The IGF-II SD scores are low in UPD7mat and IGF2mut.

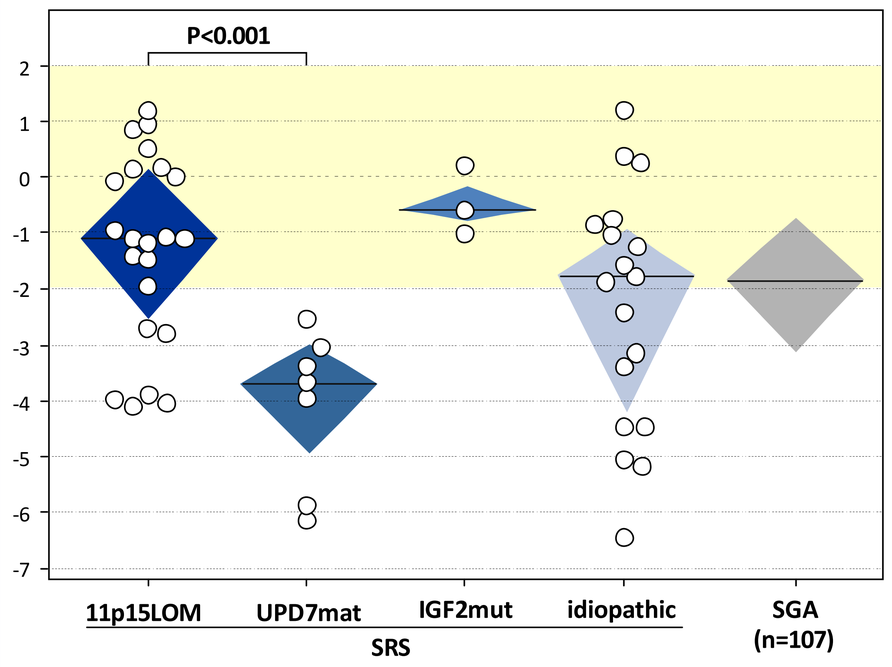

Figure 3

IGF-I SD scores: median, quartiles and individual scores.

The IGF-I SD scores are low in UPD7mat.

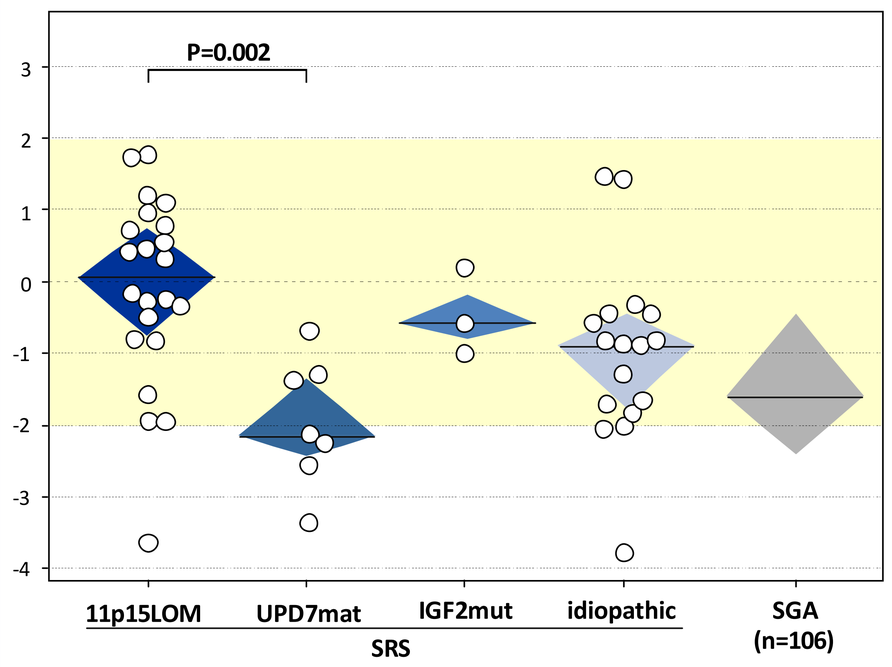

Figure 4

IGFBP-3 SD scores: median, quartiles and individual scores.

The IGFBP-3 SD scores are low in UPD7mat.

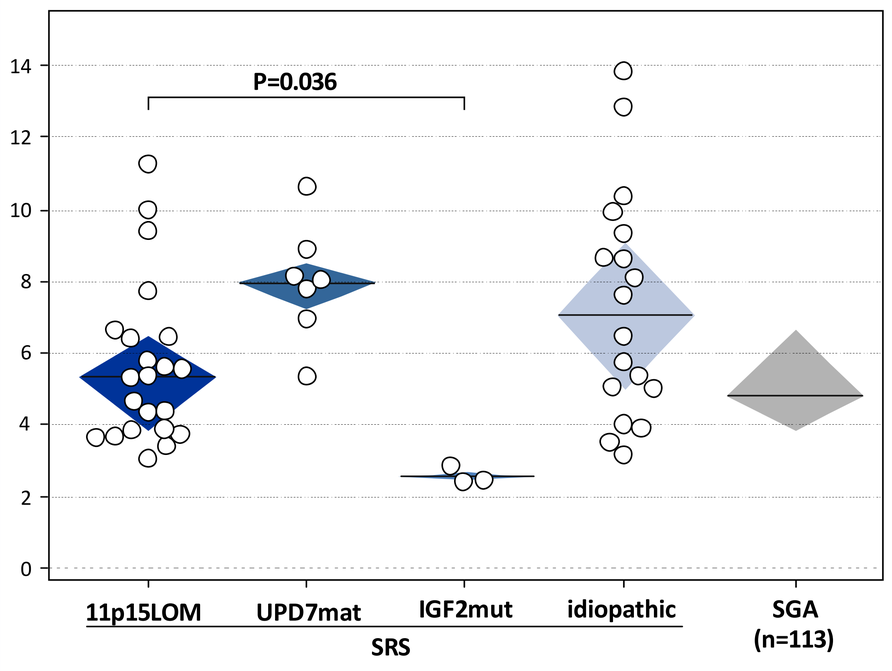

Figure 5

IGF-II to IGF-I ratio (conc/conc): median, quartiles and individual ratios.

The conc/conc ratio of IGF-II to IGF-I is very low in IGF2mut.

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