

Cross-sectional and longitudinal follow-up of changes in carbohydrate metabolism in prepubertal GH-treated SGA-patients: trends and variability; results of an unicentric study

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Conclusion:

In our collective of growth hormone (GH)-treated prepubertal SGA-patients, we found **continuously raising insulin resistance** until at least 4 years of GH-treatment. 30-min-values always were the highest. **HOMA and ISI can deteriorate independently** of each other, thus follow-up of fasting glucose and insulin levels is not sufficient. **Neither baseline nor 1-year-data for HOMA, ISI and/or oGTT are of prognostic value** for further development of glucose tolerance during GH-therapy. In our collective, temporarily pathologic values had **no therapeutic consequence**.

Background / Aims:

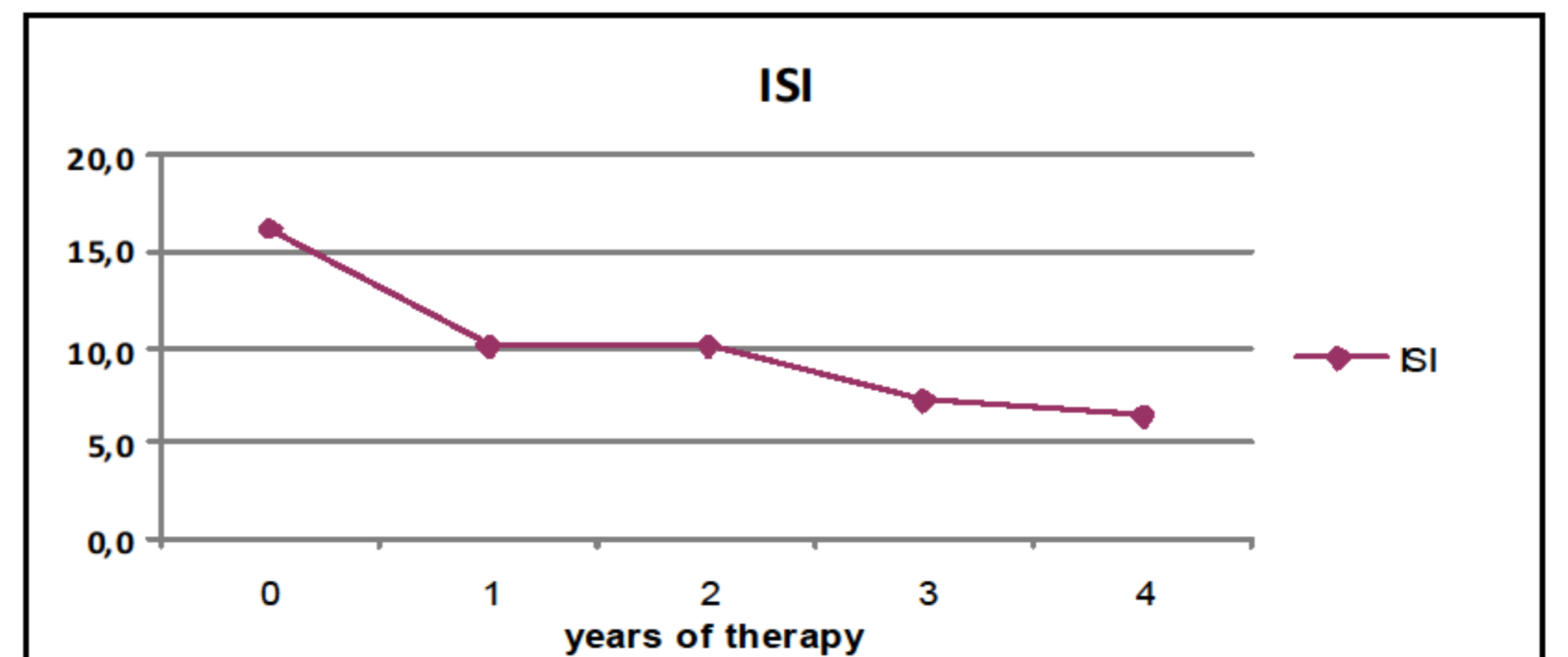
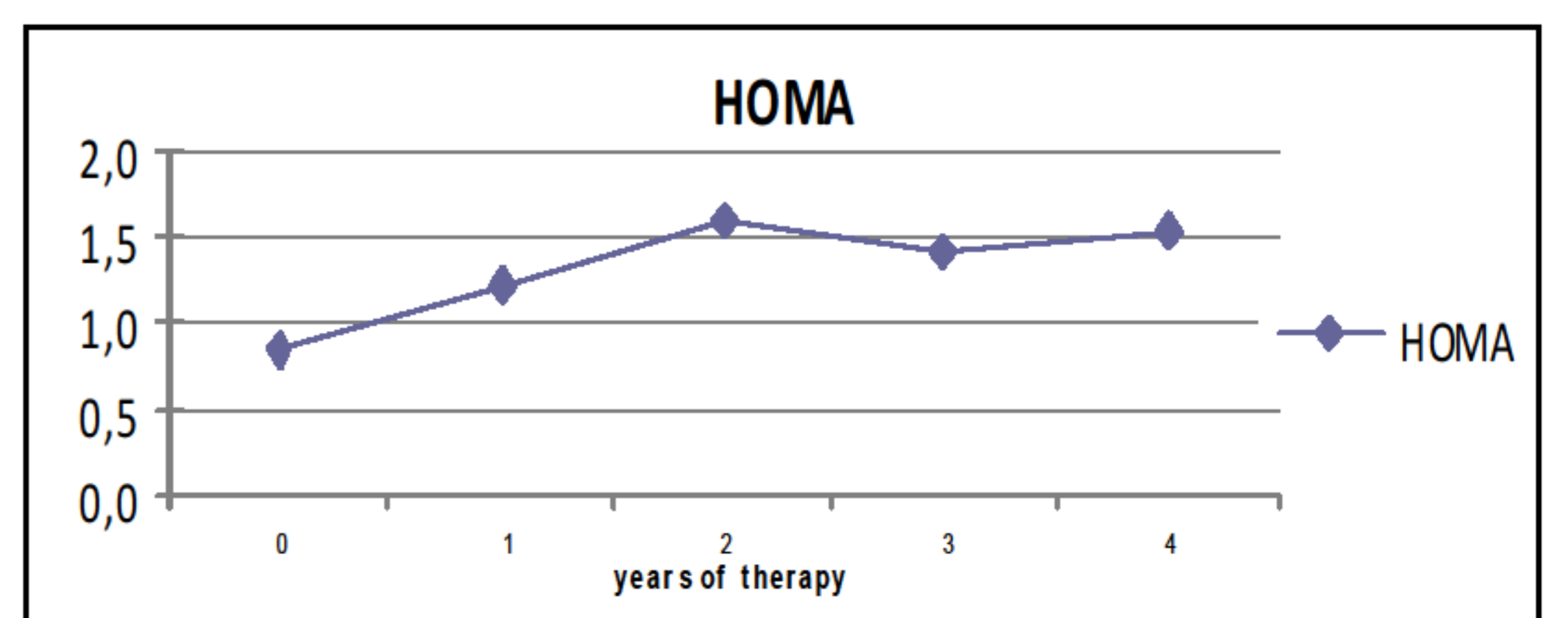
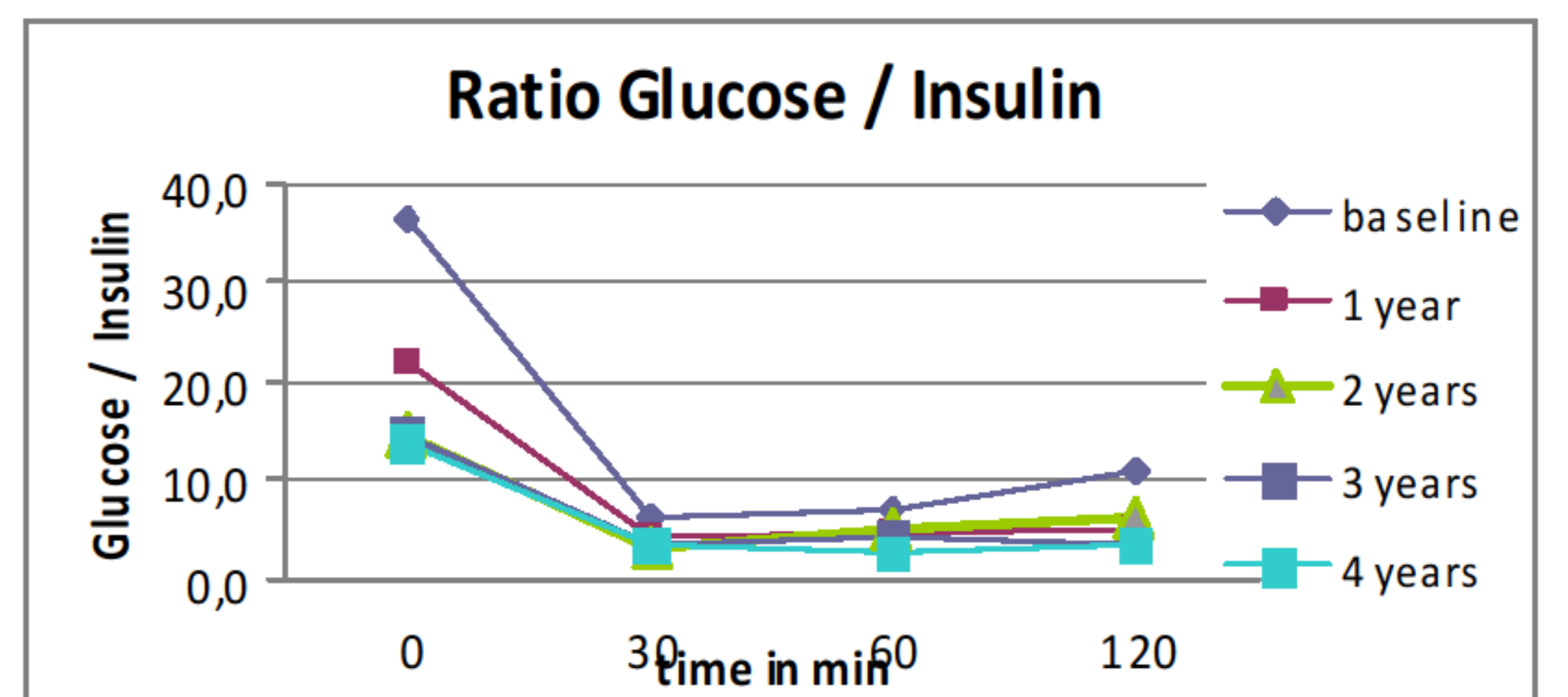
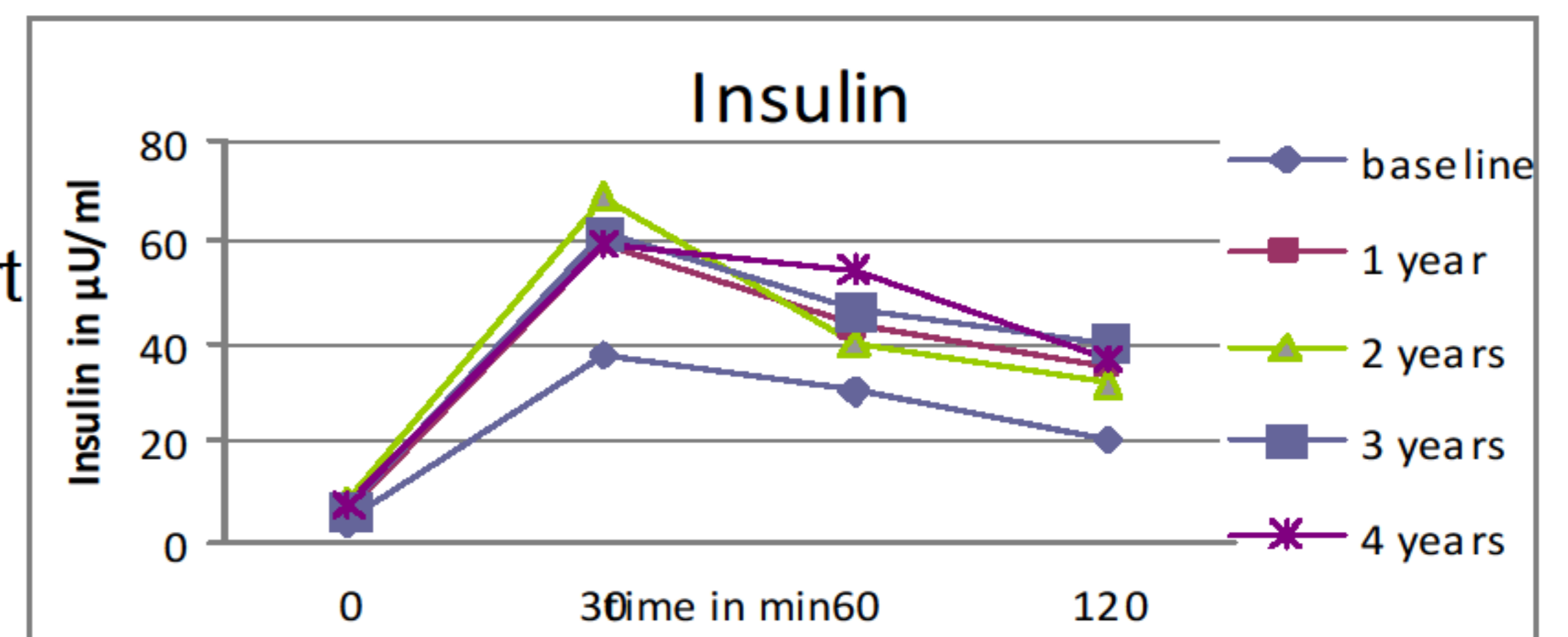
Several studies show impaired glucose tolerance at a certain number of years after start of GH in SGA-children. The aim of our investigation was to perform a longitudinal and cross-sectional evaluation of oGTTs (glucose-insulin-pairs) in prepubertal GH-treated SGA-children of our clinic, to evaluate if ISI and HOMA are effective surrogates for glucose tolerance and if results of oGTT and the indices before and after the first year of treatment are of prognostic value.

Methods:

In 86 prepubertal SGA-born children older than 4 years OGTTs (glucose and insulin at 0, 30, 60 and 120 minutes) and HOMA as well as ISI were determined before start of GH and yearly under treatment until start of puberty or max. 4 years of treatment.

Results:

- For **mean glucose-levels**, there were no relevant changes before and during the first 4 years of treatment. **Insulin-levels** significantly increased with maximum values between 1 and 3 years with little reduction thereafter. **Mean glucose/insulin-ratio** almost continuously decreased. Highest values for glucose as well as insulin were seen at 30 min in all years (not represented in ISI!). **HbA1c** was constant during all the years (5,3 +/- 0,64 to 5,4 +/- 0,24 %).
- **HOMA-indices continuously increased** during the years of treatment (0,83 +/- 0,83 to 1,53 +/- 0,98). As expected, **ISI** showed an almost inverse correlation to HOMA with **decrease from 0 to 4 years** (16,1 +/- 10,6 to 6,3 +/- 1,3). Yet, for both indices, mean values did not reach pathologic levels (HOMA > 2,5, ISI < 5).
- 3 of 81 children showed 0-min-glucose values > 100 mg/dl indicating **impaired fasting glucose (IFG)** even before GH-treatment, 7 of 81 120-min-values > 140 mg/dl (**impaired glucose tolerance, IGT**) and 3 **elevated fasting insulin** (> 10 µU/ml). None of them had pathologic oGTTs later. Only 4 of 81 had pathologic **HOMA and/or ISI** at baseline.
- **After 1 year**, 7 of 72 patients showed **IFG**, 2 had **IGT** and 5 **high fasting insulin**. 5 children showed **elevated HOMA** and 8 **decreased ISI** (mostly not the same as at 0 years). 9 of 59 **children followed for > 1 year** with any abnormal value before changed to normal. 16 of 59 with completely normal tests at 0 and 1 year showed at least one pathologic value later.



Year	Glc 0min	Glc 30min	Glc 60min	Glc 120min	Insulin 0min	Insulin 30 min	Insulin 60 min	Insulin 120min	Glc/Ins 0 min	Glc/Ins 30 min	Glc/Ins 60min	Glc/Ins 120min	HOMA	ISI	HbA1c
0	82	153	127	102	4,1	37,6	29,8	20,1	36,35	6,04	7,01	10,73	,083	16,14	5,36
1	85	152	126	105	5,6	59,3	43,1	34,4	21,82	3,90	4,53	5,03	1,21	10,11	5,39
2	82	152	116	100	7,8	68,7	39,6	31,4	14,49	3,00	4,88	5,97	1,59	10,01	5,39
3	84	153	125	101	6,7	61,8	46,4	39,4	14,58	3,23	3,92	3,41	1,42	7,20	5,36
4	82	152	114	94	7,5	58,9	53,9	36,0	13,94	3,25	2,46	3,20	1,53	6,33	5,48

Mean values for glucose (Glc), insulin, ratio glucose/insulin (Glc/Ins) for all time points of oGTT, HOMA, ISI and HbA1c for baseline (0) and years of treatment 1 to 4