Reduced mortality due to malignant neoplasms in patients receiving long-term GH replacement therapy - A Swedish study based on more than 4 000 patient-years.

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Background

Hypopituitarism in adults is associated with an excess mortality.

Untreated growth hormone (GH) deficiency has been suggested as one of the causes for the excess mortality in patients with hypopituitarism. Although, there are still safety concerns regarding the potential risk of malignant neoplasms.

Purpose

To study the mortality in adult patients with hypopituitarism caused by non-functioning pituitary adenoma (NFPA) on long-term GH replacement therapy (GHRT) or not.

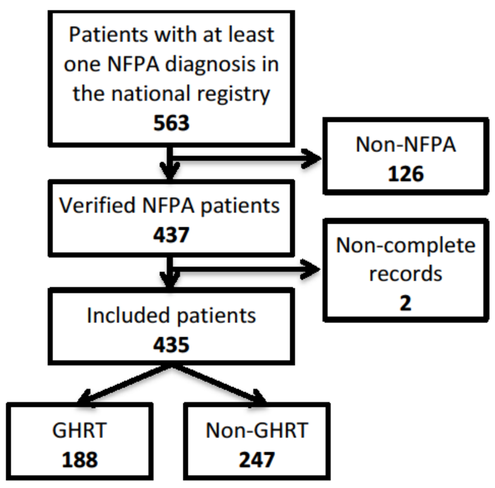

Figure 1. Inclusion of patients with non-functioning pituitary adenomas (NFPA).
Patients were identified in the Swedish National Patient Registry. GHRT = growth hormone replacement therapy was assigned to patients who were treated with GH more than 12 months.

Table 1. Characteristics of patients included in the study and number of deaths in each study group.

	GHRT	Non-GHRT
Number of patients	188	247
Men/Women (%) #	70/30	60/40
Age at diagnosis, years *	54.2 (11.7)	63.8 (15.6)
Follow-up time, years	12.6 (5.7)	7.0 (5.4)
GHRT duration, years	10.9 (6.1)	0
Cortisol replacement (%)	71	38
Levaxin replacement (%)	93	50
Sex-steroid replacement (%)	74	34
Number of deaths	15	68

Values are presented as mean±SD if not otherwise stated
*) Age at diagnosis is significantly different between the groups (p<0.001). #) Gender distribution is significantly different between the groups (p<0.05).

Table 2. Standardized mortality ratios for patients receiving GHRT or not.

	Expected no. of deaths	Observed no. of deaths	SMR	95% CI (p-value)
All patients	100.2	83	0.83	0.66-1.03 (0.09)
GHRT *	30.8	15	0.49	0.27-0.80 (0.002)
Non-GHRT *	69.3	68	0.98	0.76-1.24 (0.94)

SMR = standardized mortality rate. CI=confidence interval.
GHRT = growth hormone replacement therapy.
*) SMR differs significantly between the groups (p<0.05).

Table 3. Standardized mortality ratios for death due to malignant neoplasms

	Expected no. of deaths	Observed no. of deaths	SMR	95% CI (p-value)
All patients	25.5	13	0.51	0.27-0.87 (0.010)
GHRT	10.6	2	0.19	0.02-0.68 (0.003)
Non-GHRT	15.0	11	0.74	0.37-1.31 (0.37)

SMR = standardized mortality rate. CI=confidence interval.
GHRT = growth hormone replacement therapy.

Summary

In this study, the mortality in NFPA patients was not increased compared to the general population.

The mortality in NFPA patients receiving GHRT was reduced in comparison to non-GHRT patients despite a higher frequency of ACTH deficiency indicating a more severe disease.

Mortality due to malignant neoplasms was reduced in patients receiving GHRT.

Conclusion

GH replacement therapy in patients with NFPA was associated with a reduced overall mortality and with a reduced mortality due to malignant neoplasms.

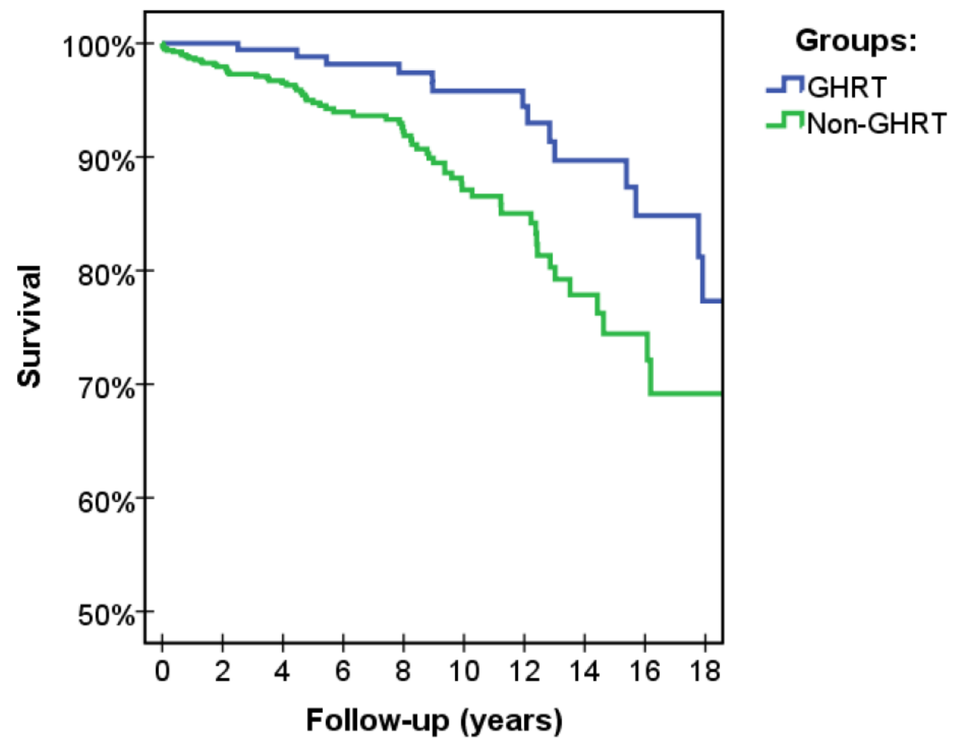

Figure 2. Cox-regression of age-adjusted mortality in patients treated with GHRT or not.
GHRT = GH replacement therapy. P=0.01 for difference in survival between patients with GHRT and non-GHRT.

Method

NFPA patients within the Sahlgrenska University Hospital's catchment-area (1.6 million inhabitants) were identified in the Swedish National Patient Registry between 1987-2011.

All records of the identified NFPA patient were reviewed (Table 1).

All patients were cross-referenced with the Swedish National Death Registry.

Standardized mortality ratios (SMRs) with 95% confidence intervals (reference: Swedish population) and cox-regression analyses were used to analyse factors influencing mortality.

Results

The SMR was not significantly different from the Swedish population in the whole group of patients with NFPA whereas it was lower than expected for the GHRT-group and as expected for the non-GHRT-group. (Table 2)

Death due to malignant neoplasms was decreased in the GHRT-group and as expected in the non-GHRT-group. (Table 3)

Cox-regression analyses (Fig 2) identified GHRT (p=0.01) and age at diagnosis (p<0.001) as factors that significantly influenced the mortality. Gender did not influence the outcome (p=0.27).

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