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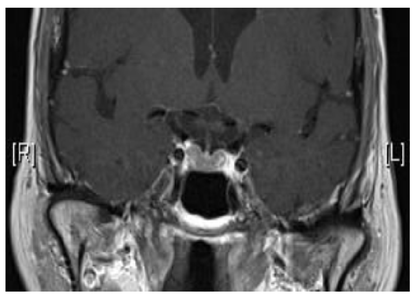
Long term follow-up of 519 patients with non-functioning pituitary adenomas from two large tertiary referral centres: a UK-Republic of Ireland collaborative study



O'Reilly MW[1], Reulen RC[2], Gupta S[3], Thompson C[3], Dineen R[3], Bugg G[1], Pearce H[1], Toogood AA[1], Gittoes NJ[1], Thompson CJ[3], Ayuk J[1].

1. Department of Endocrinology, University Hospitals Birmingham, Edgbaston, Birmingham B15 2TH, UK.
2. School of Health and Population Sciences, Unviersity of Birmingham, Edgbaston, B15 2TT, UK
3. Division of Endocrinology, Beaumont Hospital and RCSI Medical School, Dublin 9, Ireland

Background

- Non-functioning pituitary adenomas (NFPAs) are the most common subtype of pituitary tumours.
- Surgical resection, accompanied by radiotherapy (RTX) in selected cases, is the treatment of choice for compressive tumours.
- Long-term health consequences of NFPAs and their treatment are unclear.
- In this retrospective study, we aimed to assess long-term pituitary function, recurrence rates and mortality in a large NFPA cohort across two tertiary centres in the UK and Ireland.

Methods

- Case-note review of all patients treated for NFPA in Queen Elizabeth Hospital Birmingham and Beaumont Hospital Dublin between 1997 and 2012 was performed.
- Clinical presentation, imaging characteristics, pituitary function at last clinic visit and co-morbidities were recorded in each case. Data on mortality was recorded via Clinical Portal in Birmingham and via GP contact in Dublin.
- Mortality risk for internal analysis was calculated by Cox regression, and by external Poisson for comparison with general population.

Results

	Birmingham (n=271)	Beaumont (n=248)
Age at presentation (years, mean±SD)	55.9±14.3	54.5±14.0
Male	172 (63.4%)	151 (60.9%)
Follow-up duration (years, mean±SD)	8.3±5.8	8.5±6.7
Transsphenoidal surgery	90.9%	72.1%*
Tumour regrowth	34.1%	37.2%
Pituitary radiotherapy	42.4%	27.5%***
Deaths	37 (13.7%)	41 (16.5%)

Table 1: Comparison of baseline characteristics and outcome data between Birmingham and Dublin. *p<0.05; ***p<0.001

	Radiotherapy-treated (n=183)	Radiotherapy-naïve (n=336)	P-value
ACTH deficiency[1]	75.5%	58.3%	<0.001
GnT deficiency[1]	79.5%	35.1%	<0.001
TSH deficiency[1]	65.9%	46.7%	<0.001
Time to regrowth (early postop RTX only)	69.7±85.9 (n=17)	45.5±47.1	0.19
Deaths	29 (15.8%)	49 (14.6%)	0.40
Age at death	69.8±12.3	76.0±12.1	0.04

Table 2: Endocrine, recurrence and mortality data in RTX-treated and RTX-naïve patients. [1]As documented at last clinic visit.

Variable	Internal Cox adjusted for age and sex RR[1] (95% CI)	Internal Cox also adjusted for RTX RR[2] (95% CI)	External Poisson RR[3] (95% CI)
Pituitary function*	**2.31** (0.92-5.77) P=0.04	**2.24** (0.89-5.61) P=0.05	**2.23** (0.90-5.55) P=0.05
Gonadotrophin deficiency	**2.61** (1.13-6.07) P=0.01	**2.56** (1.10-5.96) P=0.01	**2.47** (1.07-5.70) P=0.02
ACTH deficiency	**2.27** (1.15-4.47) P=0.01	**2.28** (1.15-4.49) P=0.01	**2.24** (1.14-4.40) P=0.01
TSH deficiency	1.39 (0.85-2.29) P=0.18	1.38 (0.84-2.27) P=0.20	1.37 (0.80-2.16) P=0.27)
Radiotherapy	1.57 (0.97-2.54) P=0.07		1.56 (0.98-2.49) P=0.07

Table 3: Standardised mortality rates according to pituitary function. *Normal pituitary function v composite outcome of one or more deficiencies.
[1] Adjusted sex, attained age and age at diagnosis. [2] Additionally adjusted for RTX.
[3] Poisson regression incorporating the external (i.e. from the general population) mortality rates.

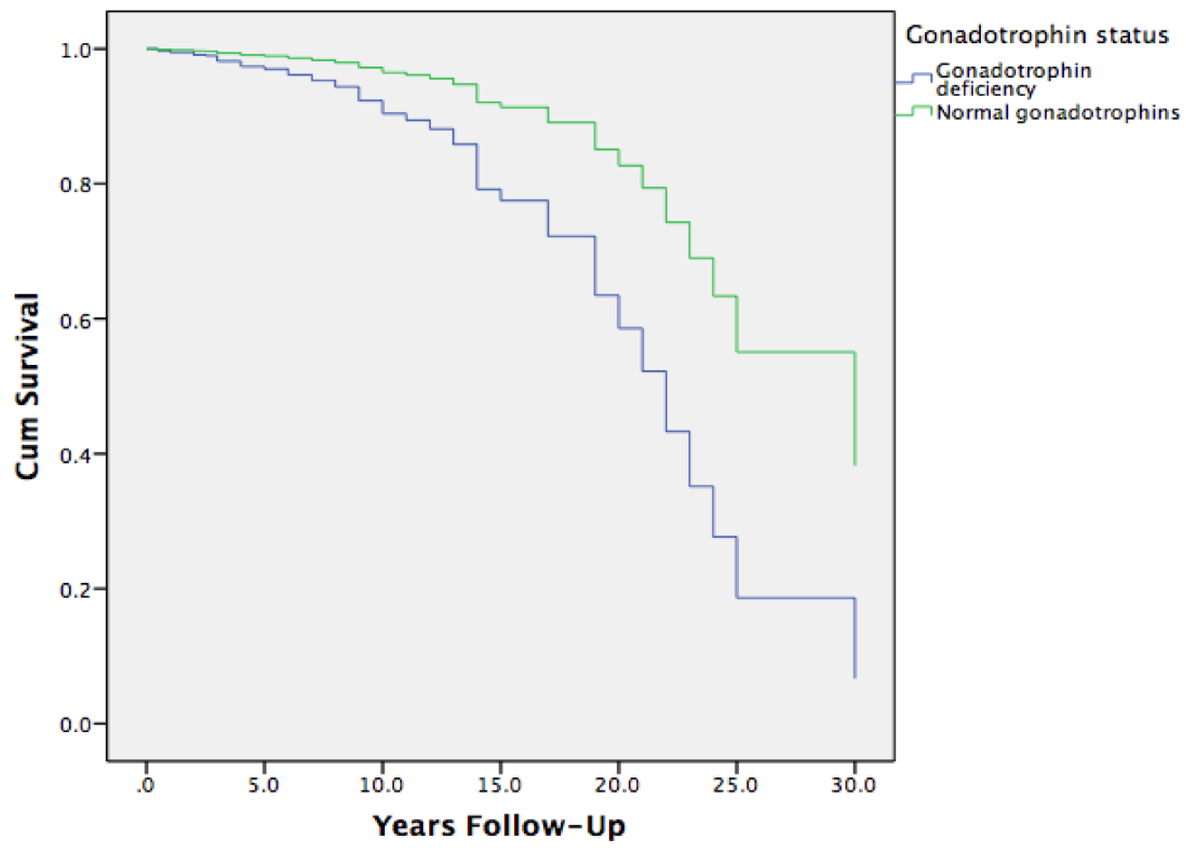


Figure 1. Survival function according to gonadotrophin status. Model adjusted for age at diagnosis, sex, ACTH def., TSH def. and RTX status.

Conclusions

- Hypopituitarism may be associated with increased mortality risk in patients treated for NFPA.
- Radiotherapy for NFPAs may not have independent effects on mortality and observed associations may be secondary to pituitary failure.
- Specifically, ACTH- and gonadotrophin-deficient patients have increased mortality risk compared to patients with intact pituitary function, and compared to the background general population.