

Gamma Knife Radiosurgery in Patients With Persistent Acromegaly or Cushing's Disease: Long-Term Risk of Hypopituitarism

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Introduction

For patient with a recurrent or residual acromegaly or Cushing's disease (CD) after resection, Gamma knife radiosurgery (GKRS) is often used. Hypopituitarism is the most common adverse effect after GKRS treatment. The paucity of studies with long-term follow up has hampered understanding of the latent risks of hypopituitarism in patients with a Acromegaly or CD. We report the long-term risks of hypopituitarism for patients treated with GKRS for Acromegaly or CD.

<u> </u>				
Parameter	Value			
Females	76.7% $(n = 46)$			
Males	23.3% ($n = 14$)			
Age (years) at the time of GKRS	41.5 (range 18–69)		
Prior Surgeries	1 (range 1-5)			
(Transsphenoidal/craniotomies), median				
Tumour parameters				
Tumour volume at GKRS (Median)	1.3 cm ³ (range 0.3-13	3.4)		
Suprasellar tumour extension	31.7% $(n = 19)$			
Cavernous sinus tumour extension	51.7% $(n = 31)$			
Radiosurgical treatment parameters				
Median margin dose (Gv)	25 (range 6-30)			
Median maximum dose (Gy)	50 (range 20-60)		
Median isodose line (%)	50% (range (30-7)	$\dot{0}$		
Median follow-up (months)	150 E ((0, 27	8)		
	159.5 (range 60–27	0)		
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Methods

From a prospectively created, IRB approved database, we identified all patients with a Acromegaly or CD treated with GKRS at the University of Virginia from 1989 to 2008. Only patients with a minimum endocrine follow up of 60 months were included. The median follow-up is 159.5 months (60.1-278). Thorough radiological and endocrine assessments were performed immediately before GKRS and at regular follow-up intervals. New onset of hypopituitarism was defined as pituitary hormone deficits after GKRS requiring corresponding hormone replacement.

Table 3. Endocrine outcomes						
Parameter			Value			
Endocrine remission						
Overall			78·396 (n	47)		
GH hypersecretion (Acromes	(aly)		75% (n = 1	18)		
ACTH hypersecretion (Cushi	ng's disease)		80.6% (n =	29)		
Hypopituitarism (all causes)			7506 (= 1	(5)		
Panhypopituitarism (all caus	(5)		10% (n)	5)		
Gamma knife induced pituitary	deficiency					
Overall			58-3% (n =	- 35)		
Median number of endocrine	e axis affected		1 (range 0-	6)		
ACTH	v denciency (overall	,	or months	(range 12-100)		
Number of patients			18·3% (n =	11)		
Median time to new ACTI	H deficiency		60 months	(range 40-160)		
Thyrotroph			25.000			
Madian time to new TSM	deficience		26-7% (<i>n</i> =	(ramos 13, 132)		
Gonadotroph	uchenery			(1110) 13 13 13 13		
Number of patients			28·3% (n =	17)		
Median time to new gonad	dotroph deficiency		60 months	(range 16-185)		
Growth hormone			33 305 (202		
Median time to new GH d	leficiency		71 months	(range 12 160)		
scuarial time to normone den	ciency after GKRS (years)	,		3	10
General (96)			10		21.7	53-3
ACTH (%)			1-7		5	12
Growth hormone (%)			2		12	27
Gonadotropin (%)			5		10	22
Parameter	ome parar	neters		Value		
Parameter	ome parar	neters		Value		
Parameter Control of tur	nour grow	rth		Value 93.3%	(n = 56)	
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Table 4. Outco Parameter Control of turn Recurrence Median time Actuarial tin 3 years 5 years 10 years Repeat GKRS Endocrine re Median time Table 5. Prognosic factors relations	nour grow to recurr to for rect emission a to remis	rth rence urrence sion ry deficiency	at GKRS	Value 93-3% (23-3% (40 mor 3% 9% 23% 23% 28-3% (70-6% (14 mor	(n = 56) (n = 14) aths (range (n = 17) (n = 12 or aths (range	ge 9–108) of 17) ge 1–74)
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Results

60 patients with either Acromegaly or CD were included. Median tumor volume at time of GKRS was 1.3 cm3 (0.3-13.4), median margin dose was 25 Gy (6-30). GKRS induced new pituitary deficiency occurred in 58.3% (n=35) of patients. Growth Hormone deficiency was most common (28.3%, n=17). The actuarial overall rates of hypopituitarism at 3, 5, and 10 years were 10%, 21.7%, and 53.3%, respectively. The median time to hypopituitarism was 61 months after GKRS (range, 12-160). Cavernous sinus invasion of the tumor was found to correlate with the occurrence of a new or progressive hypopituitarism after GKRS (p=0.018).

Conclusions

Delayed hypopituitarism increases as a function of time after radiosurgery. Hormone axes appear to vary in terms of radiosensitivity. Patients with adenoma in the cavernous sinus are more prone to develop loss of pituitary function after GKRS.

