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Research Article

Clinical Outcomes in Patients with Pituitary Adenoma Treated with Radiotherapy

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ABSTRACT

Introduction: Pituitary adenomas represent 16.2% of primary cranial neoplasms and cause significant endocrine and neurological dysfunction. While radiotherapy is used for residual, recurrent, or inoperable tumors, long-term patterns of relapse remain poorly understood.This study analysed the clinical outcomes in patients with pituitary adenoma treated with radiotherapy.

Materials and Methodology: A retrospective cohort study included 14 patients with pituitary adenoma treated with radiotherapy between January 1, 2012, and December 31, 2024 at our centre. Demographics, treatment plans, and pre-/post-radiotherapy MRI characteristics like tumor volume, cavernous sinus involvement, optic chiasm displacement were recorded. Clinical outcomes including tumor control, hormone normalization, and overall survival were analysed.

Results: Among 14 patients (6 males, 8 females; median age 55 years), headache was the most common symptom (85.7%), 11 had visual field defects, 3 had acromegaly, and 10 had functional tumors (71.4%). Macroadenoma was the predominant histology (42.9%). All patients underwent prior surgery (50% transsphenoidal). Radiotherapy was delivered primarily at recurrence (71.4%), with a median interval of 33.7 months from diagnosis. The predominant dose schedule was 50.4 Gy in 28 fractions (78.6%). Post-radiotherapy MRI demonstrated a 24.5% mean tumor volume reduction and a 50% reduction in cavernous sinus involvement and optic chiasm displacement. Median overall survival was 124 months (95% CI: 116–132), with 5-year and 10-year survival rates of 100% and 75%, respectively. Zero recurrences occurred.

Conclusions: Radiotherapy provides excellent local control and symptom relief, achieving meaningful volume reduction and structural decompression in pituitary adenomas.

Keywords: Pituitary adenoma, Radiotherapy, Survival outcomes, Cavernous sinus.

INTRODUCTION

Pituitary adenomas are the second most frequent intracranial tumour type after meningiomas, and account for 16.2% of all primary cranial neoplasms[1].They are the most common tumors of the pituitary gland and represent a significant cause of endocrine dysfunction and neurological symptoms.

The management of pituitary adenomas involves a combination of surgery, medical therapy, and, in some cases, radiotherapy. Radiotherapy is typically reserved for patients with residual or recurrent tumors after surgery or for those who are not candidates for surgery due to the tumor's location or the patient's medical condition.

Although radiotherapy is an effective treatment for controlling tumor growth and alleviating symptoms, the patterns of relapse and long-term outcomes in these patients remain poorly understood. This study analysed the clinical outcomes in patients with pituitary adenoma treated with radiotherapy in terms of tumour control, symptom relief and survival.

MATERIALS AND METHODOLOGY

Study Design and Ethics

This retrospective cohort study was conducted to evaluate the clinical outcomes in patients with pituitary adenoma treated with radiotherapy. Ethical approval for the study was granted by the Institutional Review Board (IRB No 1616/IRB-SRC/13/MCC/01-02-2025/5).

Study Population

The study population comprised all patients with a histologically confirmed diagnosis of pituitary adenoma who underwent radiotherapy—either as a primary intervention or following surgical treatment—between January 1, 2012, and December 31, 2024. Inclusion criteria were a histologically confirmed diagnosis of pituitary adenoma with history of receiving radiotherapy (primary or post-surgical) and complete clinical, radiological, and follow-up

Table 1: Histological And Imaging Characteristics Of The Pituitary Tumor

	N	%
Histology		
Pituitary macroadenoma	6	42.9
Pituitary neuroendocrine tumour	4	28.6
Silent corticotrophic adenoma	3	21.4
GH secreting macroadenoma	1	7.1
Hormonal status		
functional	10	71.4
non functional	3	21.4
Pre treatment imaging findings		
pre-treatment cavernous sinus involvement	12	85.7
Pre treatment optic chiasm involvement	14	100
Tumour location		
both sellar and suprasellar	11	78.6
sellar	2	14.3
suprasellar	1	7.1
Hardy–Wilson classification Gr 4	14	100
Knosp–Steiner classification		
Knosp 2	2	14.3
Knosp 3A	2	14.3
Knosp 4	10	71.4

records were available including tumor features, treatment specifications, and long-term follow-up details.

Study Objectives and Outcome Measures

The main objective was to evaluate clinical outcomes in this cohort, specifically -Tumor Control, defined as the absence of tumor progression or growth on follow-up cross-sectional imaging (MRI/CT), Hormone Normalization evaluated by assessment of functional hormonal response post-treatment and Overall Survival (OS), defined as the duration from the date of diagnosis to death from any cause or the date of the last follow-up.

Data Collection & Radiotherapy Parameters

Data were extracted retrospectively from physical and electronic medical records. Parameters collected included demographic characteristics, baseline tumor features (including hormonal status when available), treatment details, and follow-up clinical data. Specific radiotherapy planning parameters and delivery details were retrieved directly from the Treatment Planning System (TPS).

Radiological Assessment and Volumetric Analysis

Pre- and post-radiotherapy MRI scan images were reviewed to record tumor extent (sellar, suprasellar, or both) and involvement of adjacent critical structures, specifically optic chiasm displacement and cavernous sinus invasion. Longitudinal changes in adjacent structure involvement or displacement were recorded.

The tumours were classified according to the Hardy–Wilson classification system which evaluated sellar destruction based on its severity (grade) and the extent of extrasellar extension (stage) and Knosp– Steiner classification for evaluation of cavernous sinus invasion based on coronal T1-weighted contrast imaging[2].

Tumor volume was calculated assuming a roughly spherical or ellipsoidal shape using the standard ellipsoid formula, $V = (dcc \times dap \times dl \times \pi) / 6$, where dcc, dap, and dl are the craniocaudal, anteroposterior, and lateral diameters, respectively, measured on cross-sectional images[3]. The quantitative difference between pre- and post-radiotherapy volumes was evaluated for each patient.

Outcome Measures:

Outcome measures included Tumor Control, defined as absence of tumor progression or growth on follow-up imaging (MRI/CT) and Overall Survival (OS) defined as time from diagnosis to death from any cause/ last date of follow up.

Generative AI (Google Gemini) was utilized exclusively for language editing and text polishing during manuscript preparation. All clinical data, statistical analyses, and final prose were independently verified and finalized by the primary authors.

Statistical Analysis:

Descriptive Statistics was used for summarizing patient demographics, tumor characteristics, treatment protocols, and outcomes. Kaplan-Meier Survival Analysis was used for estimating tumor control rates and overall survival.

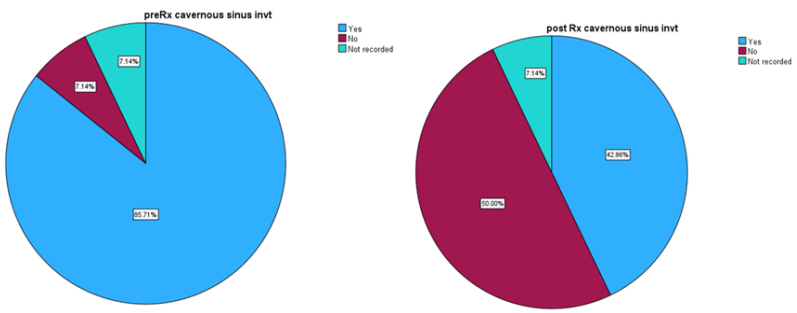


Figure 1: Frequency of cavernous sinus involvement pre (left) and post radiotherapy (right)

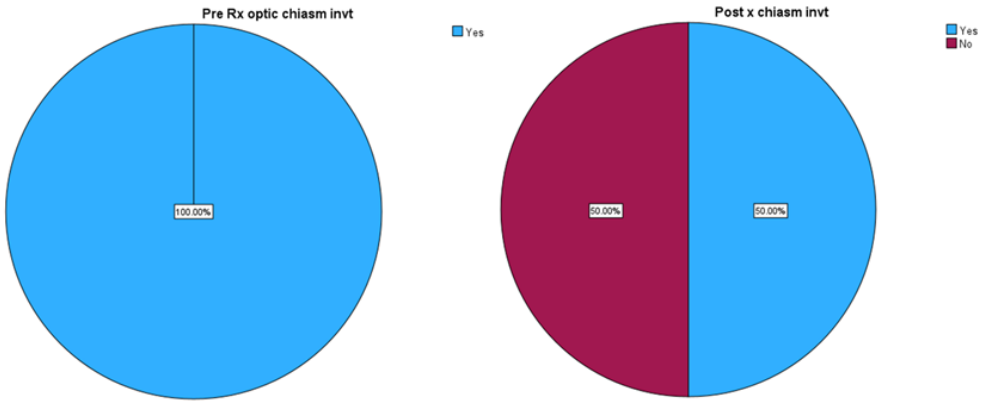


Figure 2: Frequency of optic chiasm involvement pre (left) and post radiotherapy (right)

RESULTS

Between 1st January 2012 and 31st December 2024, a total of 14 patients received radiotherapy for pituitary adenoma.

Demographic characteristics

The median age at diagnosis was 55 years (range: 27–68 years). Females constituted a slight majority of the cohort, accounting for 57% of patients (n=8), while males represented 43% (n=6). The most common baseline medical comorbidities identified were diabetes mellitus (57%, n=8), hypertension (50%, n=7), and hypothyroidism (43%, n=6). Coronary artery disease (CAD) was documented in 28.6% of patients (n=4), while other miscellaneous comorbidities were present in 28.6% (n=4). Additionally, one patient presented with bilateral optic atrophy prior to treatment.

Symptoms at presentation

Headache was the most common symptom (n=12, 85.7%). Eleven patients (78.6%) had visual field defects at presentation. Acromegaly was reported in 3 (21.4%) patients.

Tumour characteristics

The histological and imaging characteristics of the pituitary tumor in the study population are given in Table 1.

Histology

The most common histology reported was pituitary macroadenoma (42.9%). Four patients had pituitary neuroendocrine tumour. Other uncommon histologies included silent corticotrophic adenoma and growth hormone secreting macroadenoma.

Functional tumors accounted for 71.4% of cases (n=10). The most common hormonal dysfunctions were elevated adrenocorticotropic hormone (ACTH; n=4) and thyroid-stimulating hormone (TSH; n=4).

Radiology

Radiologically, the majority of lesions demonstrated sellar tumors with suprasellar extension. Tumor confined strictly to the sella was observed in two patients, while one patient presented with an isolated suprasellar tumor location. According to the Hardy-Wilson

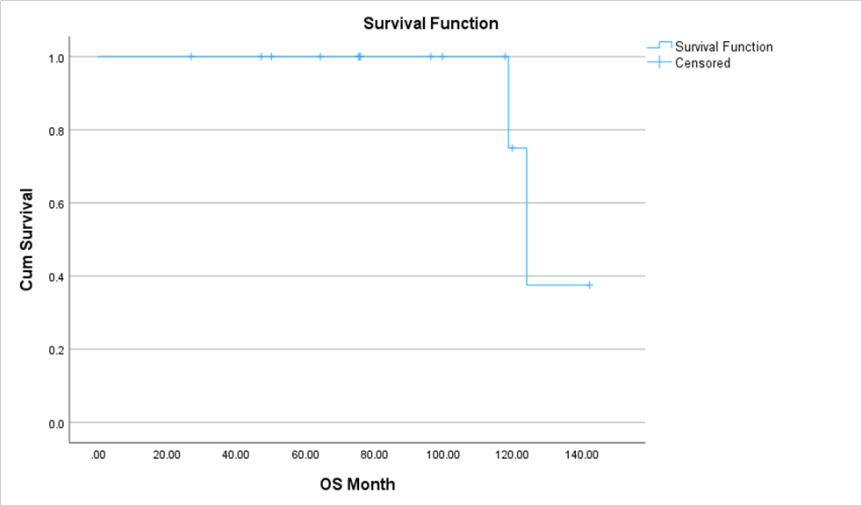


Figure 3: Kaplan Meier survival curve for overall survival in patients with pituitary adenomas

classification, all patients (100%) had Grade 4 disease. Evaluation using the Knosp-Steiner classification revealed that the majority of lesions were Knosp Class 4 tumors (71.4%, n=10). Baseline pre-radiotherapy imaging showed optic chiasm involvement in all 14 patients (100%), with cavernous sinus invasion also identified in the majority of the study population.

Treatment details

All patients (n=14) underwent surgical resection prior to radiotherapy. The most common surgical approach was transsphenoidal surgery (50%, n=7), followed by open craniotomy (21.4%, n=3); surgical approach was unrecorded in four patients (28.6%). Regarding timing, the majority of patients received radiotherapy for disease recurrence following surgery (71.4%, n=10), while four patients (28.6%) received adjuvant postoperative radiotherapy. Among those treated for relapse, three patients received radiotherapy at first recurrence. Prior to initiating radiotherapy, five patients had undergone two surgical procedures, and one patient had undergone three surgeries. The overall time interval between the initial surgical intervention and the start of radiotherapy ranged from 2 to 49 months, with a median interval of 5 months. Among patients who received radiotherapy specifically at disease recurrence (n=10), the median time gap between surgery and the commencement of radiotherapy was 10 months (range: 5 to 49 months).

The median time from initial diagnosis to the start of radiotherapy was 33.7 months (range: 2.8–114.3 months; interquartile range [IQR]: 78.02 months). The predominant radiation regimen was 50.4 Gy delivered in 28 fractions (78.6%, n=11), while the remaining three patients received 54 Gy in 30 fractions (21.4%). The majority of patients were treated using Volumetric Modulated Arc Therapy (VMAT; 85.7%, n=12).

Tumor Volumetric and Structural Response

Pre-radiotherapy MRI demonstrated a mean tumor volume of 13.3 cc (95% confidence interval 1.3 cc to 25.4 cc) and a median volume of 7 cc (range: 0.6 - 77.2 cc, IQR -10.48). Follow-up cross-sectional imaging post-radiotherapy revealed a reduction in tumor dimensions, with a mean post-treatment volume of 7 cc (95% CI 2.2 - 11.9) and a median post-treatment volume of 3 cc (range: 0.2–29.1, IQR 5.89).

The mean percentage reduction in tumor volume following radiotherapy was 24.5% (95% CI -8.7 % to 57.8%). However, this quantitative volumetric reduction did not reach statistical significance ($p = 0.45$). The median time interval to document radiological response on follow-up imaging post-radiotherapy was 7.2 months (range: 3.6–33.2 months, IQR 7.05).

Regarding local structural invasion, baseline pre-radiotherapy imaging showed cavernous sinus involvement in 12 patients (85.7%). Following radiotherapy, persistent cavernous sinus involvement was documented in only 6 patients (42.9%), representing a 50% overall regression in cavernous sinus invasion (Figure 1).

All patients (100%, n=14) demonstrated optic chiasm displacement on pre-radiotherapy imaging. Following treatment, post-radiotherapy imaging confirmed complete resolution of optic chiasm displacement in half of the cohort (50%, n=7) (Figure 2).

Overall survival

The median overall survival was 124 months (95% CI 116 -132 m). The overall survival was 100% at 5 years and 75% at 10 years. The Kaplan-Meier survival curve for overall survival is shown in Figure 3. None of our patients had recurrence.

DISCUSSION

Pituitary adenomas are among the most common primary intracranial neoplasms, second in frequency only to meningiomas[4]. Although pathologically benign, macroadenomas frequently cause significant pressure effects on adjacent critical structures, requiring multimodal management. Primary therapeutic strategies include surgery, medical therapy, and radiotherapy. Radiotherapy is primarily indicated for patients with significant symptomatic residual disease following primary surgery, those with disease recurrence not amenable to repeat surgical resection, or individuals who are medically unfit for surgical intervention[5]. Radiotherapy plays a critical role in alleviating intracranial symptoms, particularly visual field deficits and cavernous sinus compression. The aim of the present study was to analyze clinical outcomes and relapse patterns in patients with pituitary macroadenomas treated with radiotherapy at our center; hence, our cohort was comprised exclusively of macroadenomas.

In general, pituitary macroadenomas exhibit a higher prevalence in females[6]. However, gender distribution varies depending on the specific hormonal subtype; for instance, prolactinomas are more common in females, whereas growth hormone (GH)-secreting adenomas occur more frequently in males. The incidence of pituitary adenomas increases with age, peaking between the third and sixth decades of life (30 to 50 years). In an epidemiological study by McDowell et al. evaluating demographic differences in pituitary adenoma incidence, the authors observed that incidence rates generally increased with age, peaking in the fifth to seventh decades, with a female predominance in early life and a male predominance in later years[7]. A similar demographic pattern was observed in our cohort, which demonstrated a higher frequency among females and a median age of 55 years.

Pituitary adenomas have been shown to cause substantial cardiovascular morbidity and excess mortality[8]. Similarly, Hammarstrand et al. reported an increased risk of type 2 diabetes mellitus in patients without growth hormone replacement therapy (GHRT)[9]. Secretory adenomas manifest with distinct clinical phenotypes (including acromegaly/gigantism, Cushing's disease, and prolactinomas) dictated by the specific hormone hypersecreted[10]. In our study, 57% of patients had diabetes mellitus, 28.6% had coronary artery disease, and 43% had hypothyroidism.

Visual impairment is reported in approximately 40% to 60% of patients with pituitary macroadenomas[11]. Suprasellar extension causing compression of the optic chiasm frequently leads to visual field deficits, with bitemporal hemianopia being the most prevalent pattern, followed by homonymous defects. Headache, although a non-specific symptom, is also commonly reported[12]. Correspondingly, headache and visual field defects constituted the most frequent presenting symptoms in our patient cohort.

Non-functioning pituitary macroadenomas are generally more prevalent than functional tumors, with an estimated population prevalence of 7 to 41.3 cases per 100,000 and an annual incidence of 0.65 to 2.34 cases per 100,000[13]. However, the majority of tumors in our study were functional macroadenomas. Because our study included only patients who underwent radiotherapy, this selection criteria inherently masked the true institutional ratio of functional to non-functional tumors. These patients were specifically referred for radiotherapy due to persistent disease symptoms and/or lack of further surgical options.

In a study by Sarah E. Nicholas et al., evaluating outcomes in non-functioning pituitary macroadenomas managed by delaying radiation therapy until disease progression post-debulking surgery, the majority of observed patients did not require further intervention for five or more years, and half remained intervention-free for ten or more years[14]. A comparable prolonged interval between initial diagnosis and radiation intervention was noted in our study, with a median time of 33.7 months from diagnosis to radiotherapy initiation.

A primary objective of radiation therapy in pituitary adenomas is to arrest tumor growth, with partial regression reported in approximately two-thirds of cases[15]. In a study by Ferah Yildiz et al. examining radiotherapy in the management of giant pituitary adenomas, improvements in visual acuity and visual fields were achieved in 63% of patients[16]. In our cohort, all patients had Grade 4 disease according to the Hardy-Wilson classification, and the majority had Knosp Class 4 involvement, with 100% displaying baseline optic chiasm displacement and the majority demonstrating cavernous sinus invasion. Following radiotherapy, patients experienced clinical symptom relief paired with evident radiological response. The mean percentage reduction in tumor volume was 24.5%, accompanied by a 50% reduction in both cavernous sinus involvement and optic chiasm displacement.

Gittoes et al. compared treatment outcomes between surgery alone and surgery followed by postoperative radiotherapy, reporting 10-year progression-free survival rates of 68% and 93%, respectively[17]. In our cohort, the 10-year overall survival rate was 75%, with no disease recurrences documented during the follow-up period. These findings underscore the crucial role of radiotherapy in achieving durable disease control in pituitary macroadenomas.

LIMITATIONS

The main limitation of our study is its small sample size. Furthermore, because inclusion was restricted to patients who received radiotherapy, the data are not representative of pituitary macroadenoma management as a whole. Following completion of radiotherapy, the majority of patients were followed up primarily by endocrinologists or neurosurgeons, limiting our direct access to long-term post-radiotherapy hormonal normalization data. However, serial post-radiotherapy MRI imaging was successfully retrieved for the majority of patients. Future prospective, multicenter studies involving larger patient cohorts and dedicated multidisciplinary collaboration among neurosurgeons, endocrinologists, and radiation oncologists will help provide a more comprehensive understanding of these tumors.

CONCLUSIONS

The clinical and demographic characteristics of our study population—including age, gender distribution, and presenting symptoms—align with established literature data. Radiotherapy achieved a favorable clinical and radiological response in pituitary macroadenomas, as evidenced by effective symptom control, a mean tumor volume reduction of 24.5%, and a 50% regression in cavernous sinus involvement and optic chiasm displacement.

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