

Pituicytoma Cases - Correlating Radiological, Pathological, and Surgical Outcomes: A systematic review and meta-analysis

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Abstract

Introduction: Pituicytomas are rare glial neoplasms originating from the neurohypophysis, often posing diagnostic and therapeutic challenges due to their nonspecific imaging features and limited case series in the literature. Their biological behavior, optimal management, and prognostic factors remain poorly defined.

Objective: This systematic review and meta-analysis aim to synthesize available evidence on radiological, pathological, and surgical outcomes in pituicytoma, evaluating diagnostic accuracy and outcome predictors.

Method: A comprehensive search was conducted using PubMed, Embase, Scopus, and Cochrane Library databases for studies published up to 2025. Included studies reported radiological findings (MRI, CT, [^{18}F]FET PET/MRI, angiography), histopathological markers, and surgical outcomes. Data on diagnostic modalities, imaging characteristics, immunohistochemical profiles, surgical approaches (transsphenoidal, transcranial, endoscopic), and outcomes (recurrence, progression, remission) were extracted. Data were extracted and analyzed using random-effects models due to expected heterogeneity. Random-effects meta-analysis assessed pooled recurrence rates, with heterogeneity evaluated via I^2 statistics.

Results: A total of 233 articles were identified using predefined search terms. Four studies totaling 151 cases were included. Pituicytomas were predominantly sellar/suprasellar, isointense on T1-weighted MRI, hyperintense on T2-weighted MRI, and intensely enhancing. [^{18}F]FET PET/MRI showed 100% sensitivity for small functional tumors. Histopathologically, TTF-1, S100, and GFAP were consistently expressed. Gross-total resection (GTR) was achieved in 54.5–61% of cases, with a pooled recurrence rate of 4.9% (95% CI: 1.2–15.5%) versus 35.2% (95% CI: 22.7–49.8%) for non-GTR ($\text{Tau}^2 = 0.1821$, $I^2 = 45.3\%$, $P = 0.1395$). Transsphenoidal surgery increased progression risk (HR: 3.559, 95% CI: 1.015–12.476). Male gender and tumor diameter ≥ 1.85 cm predicted progression. Complications included endocrine abnormalities (18.2%).

Conclusion: Pituicytoma remains diagnostically challenging due to nonspecific imaging and clinical overlap with other sellar neoplasms. This meta-analysis underscores the diagnostic value of TTF-1 immunohistochemistry, supported by MRI features. Advanced imaging modalities such as [^{18}F]FET PET/MRI may further improve preoperative identification. Moderate heterogeneity suggests variability in outcomes, supporting tailored surgical strategies and long-term follow-up.

INTRODUCTION

Pituicytoma is an uncommon, low-grade glioma that arises from pituicytes in the neurohypophysis or infundibular stalk, representing a rare subset of central nervous system tumors.¹ First described in the mid-20th century, pituicytomas are typically slow-growing and benign, classified as World Health

Organization (WHO) Grade I neoplasms.^{2,3} Clinically, these tumors often present with symptoms related to mass effect, such as visual disturbances or hypopituitarism, owing to their predilection for the sellar and suprasellar regions.⁴ The rarity of pituicytoma, has contributed to ongoing challenges in establishing standardized diagnostic and management protocols.⁵ They typically present in middle-aged adults, often mimicking more common sellar masses like pituitary adenomas or meningiomas. Their benign nature belies the diagnostic and therapeutic challenges they pose due to their location and vascularity.⁶

Radiologically, pituicytomas present with non-specific features that frequently overlap with other sellar and suprasellar masses.⁷ On magnetic resonance imaging (MRI), these tumors are typically isointense on T1-weighted images and hyperintense on T2-weighted images, with robust and homogeneous contrast enhancement.⁸ Advanced imaging, such as [¹⁸F]FET PET/MRI, has shown high sensitivity for detecting small functional tumors, particularly in cases with inconclusive standard MRI.⁹ Angiography often reveals a rich vascular supply from superior hypophyseal arteries.¹⁰ These features, while distinctive, overlap with other sellar pathologies, complicating preoperative diagnosis. Accurate imaging is essential for surgical planning

Surgically, gross-total resection (GTR) is the preferred approach, achieving lower recurrence rates compared to subtotal resection. The pituicytomas are approached via transsphenoidal or transcranial routes, with GTR being the treatment of choice.¹¹ These tumors are characteristically hypervascular, which increases the risk of intraoperative bleeding and may complicate complete removal.¹² Histopathologically, pituicytomas display spindle or oval cells in fascicular arrangements and are immunoreactive for thyroid transcription factor-1 (TTF-1), S100, and variably for glial fibrillary acidic protein (GFAP). TTF-1 nuclear positivity is considered a highly sensitive and specific marker, distinguishing pituicytoma from other sellar gliomas and pituitary adenomas. The Ki-67 proliferation index is typically low, supporting the indolent nature of these tumors.¹³

Despite increasing recognition, significant gaps persist in the literature regarding the optimal diagnostic algorithm, prognostic factors, and long-term outcomes for pituicytoma.¹⁴ Most published data are derived from isolated case reports or small case series, limiting the generalizability of findings and precluding robust evidence-based recommendations.¹⁵ The overlap in imaging and clinical presentation with other sellar lesions further complicates preoperative diagnosis, often necessitating reliance on histopathological and immunohistochemical confirmation.¹⁶ Additionally, the risk factors for recurrence and the impact of surgical approach on prognosis remain incompletely defined. These limitations highlight the need for comprehensive analyses.

Given these uncertainties, the objective of this study is to systematically review and meta-analyze published cases of pituicytoma, focusing on the correlation between radiological findings, pathological markers expression and surgical outcomes.

METHODOLOGY

Study Design

This systematic review and meta-analysis were conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to ensure rigorous and transparent reporting. The study aimed to synthesize data on pituitaryoma cases, correlating radiological, pathological, and surgical outcomes. A predefined protocol was registered with PROSPERO to guide the research process, outlining eligibility criteria, search strategies, and analytical methods.

Literature Search Strategy

A comprehensive electronic search was performed across multiple databases including PubMed (MEDLINE), Embase, Web of Science Core Collection, Scopus, and the Cochrane Central Register of Controlled Trials (CENTRAL), using the following time frame: from database inception up to 2025. Search strategies were developed using a combination of controlled vocabulary (MeSH terms) and free-text keywords, encompassing both tumor-specific and outcome-related terminology. Key search terms included: "pituitaryoma," "neurohypophysis tumor," "sellar glioma," "radiological features," "histopathology," and "surgical outcomes." Reference lists of included studies were hand-searched to identify additional relevant articles.

Eligibility Criteria

Studies were included if they: (1) reported histopathologically confirmed pituitaryoma cases; (2) provided data on radiological findings (MRI, CT, [¹⁸F]FET PET/MRI, or angiography), histopathological markers (TTF-1, S100, GFAP), or surgical outcomes (gross-total resection [GTR], recurrence, complications); and (3) were observational studies, case series, or case reports. Exclusion criteria encompassed non-human studies, reviews without original data, and studies lacking sufficient detail on outcomes or diagnostics. Duplicates or overlapping datasets. Non-English publications without full-text access or available translation. Two reviewers independently screened titles, abstracts, and full texts, resolving discrepancies through consensus.

Data Extraction

Data were extracted using a standardized form, capturing: (1) study characteristics (author, year, design, sample size); (2) radiological features (tumor location, MRI signal intensity, enhancement patterns); (3) histopathological markers (immunohistochemical profiles, Ki-67 index); (4) surgical details (approach, extent of resection); and (5) outcomes (recurrence rates, progression-free survival, complications). Missing data were addressed by contacting corresponding authors. Two reviewers performed extraction, with a third resolving inconsistencies. All extracted data were entered using Excel, with regular validation checks to ensure accuracy.

Quality Assessment

The methodological quality of included studies was assessed using the Newcastle-Ottawa Scale (NOS). Each study was scored based on criteria including representativeness of the sample, ascertainment of exposure/outcome, and adequacy of follow-up. Only studies scoring above a predefined threshold (Studies scoring ≥ 6 on the NOS) were considered for quantitative synthesis.

Statistical Analysis

Statistical analyses were performed using PSPP (public domain software) and METAANALYSISONLINE (<https://metaanalysisonline.com/>). Given the anticipated heterogeneity among studies due to differences in patient populations, surgical techniques, and follow-up durations, a random-effects model was employed for all pooled estimates. Outcome measures included: pooled proportions of GTR, incidence of postoperative complications, and recurrence rates. Heterogeneity was quantified using I^2 statistics and Cochran's Q test, with $I^2 > 50\%$ indicating substantial heterogeneity. Subgroup analyses were conducted based on tumor location (suprasellar vs. intrasellar/hypothalamic), surgical approach (transsphenoidal vs. transcranial), and immunohistochemical markers. Sensitivity analyses were performed by excluding low-quality studies and by one-study removal to assess robustness of results. Quantitative results were presented in forest plots, with 95% confidence intervals (CI) and p-values reported.

Ethical Considerations

As a systematic review, no primary patient data were collected, and ethical approval was not required. All included studies were evaluated for ethical compliance, ensuring patient consent and institutional review board approvals were reported where applicable. Data synthesis adhered to principles of transparency and reproducibility.

RESULTS

A detailed summary of the search process is outlined in the PRISMA flow diagram (Fig. 1), which illustrates the sequential stages involved in identifying and selecting studies for this systematic review. Initially, a total of 233 records were retrieved from electronic databases using a predefined set of search terms. After eliminating duplicates and excluding non-relevant items such as review articles, editorials, commentaries, case reports, and abstracts that did not provide adequate clinical or methodological detail, 171 unique studies remained for further evaluation.

These remaining articles underwent title and abstract screening, followed by a full-text assessment based on relevance criteria. The inclusion decision focused on studies that investigated pituicytoma in relation to radiological characteristics, histopathological findings, and surgical outcomes. After applying

the inclusion and exclusion criteria, four studies satisfied all requirements and were ultimately selected for comprehensive data extraction and subsequent analysis.

All selected studies explored the link between pituitary case correlating radiological, pathological, and surgical outcomes. Of the four studies that met the inclusion criteria, all presented univariate analysis and multivariable analysis of the data. The studies were conducted across various countries, with sample sizes ranging from 3 to 115 participants.

Characteristics of the included studies

An overview of the studies included in this review is presented in Table 1, while Table 2 summarizes the main methodological and demographic characteristics across the selected investigations.

Table 1. Overview of the included studies

Study	Author	Year	N cases	Diagnostic Modality	Key Imaging Features	Histopathological Markers	Surgical Approach	Outcome Measure
1	Chen, et al. ¹⁷	2021	3	MRI, Histopathology	Variable, sellar/suprasellar mass, isointense T1, hyperintense T2	TTF-1, GFAP, S100	Transsphenoidal, transcranial	Recurrence rate not specified
2	Pruis, et al. ⁹	2024	22	[¹⁸ F]FET PET/MRI	All patients had a positive [¹⁸ F]FET PET/MRI result	Not specified	Surgery, Gamma Knife, CyberKnife	High short-term remission rate of 75%.
3	Wei, et al. ¹¹	2021	115	MRI, Histopathology	Sellar/suprasellar, isointense T1, hyperintense T2	TTF-1, S-100, vimentin, GFAP, EMA, synaptophysin, and Ki-67	Transcranial, transsphenoidal	Recurrence = 27.3%
4	Cheng, et al. ¹⁸	2021	11	MRI, Histopathology	Sellar/suprasellar, isointense T1, hyperintense T2	S100, vimentin, GFAP, TTF-1 and EMA	Endoscopic transsphenoidal or craniotomy	Tumor progression after surgical resection occurred in 36.4%

Table 2. General characteristics of the studies included.

Study	Type of study	Objective	N cases	Conclusion
Chen B et al. ¹⁷	Case reports and literature review	Reported cases of histopathologically diagnosed pituitary tumor	A review of 168 pituitary tumor cases and 3 case reports	"Pituitary tumor: rare glioma with distinct imaging, pathology, and surgical management."
Pruis IJ et al. ⁹	Retrospective study	Evaluate [¹⁸ F]FET PET/MRI diagnostic yield, sensitivity, positive predictive value for pituitary tumors; compare with MRI, petrosal sinus sampling, follow-up.	22	"[¹⁸ F]FET PET/MRI shows a high diagnostic yield for localizing small functional pituitary tumors."
Wei LD et al. ¹¹	systematic review and meta-analysis	To assess the risk factors for pituitary tumor progression and then to propose the optimal treatment algorithm.	115	"Based on our findings, GTR was advocated as an optimal treatment for pituitary tumors."
Cheng JH, et al. ¹⁸	Study retrospectively	To evaluate the clinical, radiological, pathological, and prognostic features of pituitary tumor in order to enhance understanding of its diagnostic challenges, optimal treatment strategies, and predictive factors for outcome.	11	"Currently, GTR is the best approach for the treatment of pituitary tumors. More patients and longer follow-up periods were needed to further elucidate the biological features of pituitary tumors."

The methodological quality of included studies was evaluated using the Cochrane Collaboration's revised Risk of Bias 2 (RoB 2) tool, which assesses bias through domain-specific signaling questions and algorithm-driven judgments. The evaluation revealed predominantly low risk of bias across studies. Detailed evaluations, demonstrate in Figures 2-3, highlighted variability in bias profiles.

Meta-analysis

This study applied a methodologically rigorous meta-analytical framework to systematically evaluate pituitaryoma cases, emphasizing the integrative analysis of radiological characteristics, pathological marker expression, and surgical outcomes. An exhaustive and strategically designed literature search was executed, encompassing all relevant publications available up to the year 2025. To maximize comprehensiveness, multiple leading bibliographic databases-including PubMed (MEDLINE), Embase, Web of Science Core Collection, Scopus, and the Cochrane Central Register of Controlled Trials (CENTRAL)-were meticulously queried using tailored search algorithms. This approach ensured the inclusion of a broad spectrum of pertinent studies, thereby underpinning the robustness and validity of the synthesized evidence.

The meta-analysis incorporated four studies that systematically examined cases of pituitaryoma, with a particular focus on synthesizing radiological features, pathological marker profiles, and surgical outcome data.

A total of 233 articles were identified using predefined search terms. Four studies totaling 151 cases were included. Pituitaryomas were predominantly sellar/suprasellar, isointense on T1-weighted MRI, hyperintense on T2-weighted MRI, and intensely enhancing. [^{18}F]FET PET/MRI showed 100% sensitivity for small functional tumors. Histopathologically, TTF-1, S100, and GFAP were consistently expressed. Gross-total resection (GTR) was achieved in 54.5–61% of cases, with a pooled recurrence rate of 4.9% (95% CI: 1.2–15.5%) versus 35.2% (95% CI: 22.7–49.8%) for non-GTR ($\text{Tau}^2 = 0.1821$, $I^2 = 45.3\%$, $P = 0.1395$) (Fig. 4). Transsphenoidal surgery increased progression risk (HR: 3.559, 95% CI: 1.015–12.476). Male gender and tumor diameter ≥ 1.85 cm predicted progression.

DISCUSSION

Pituitaryomas, rare glial neoplasms of the neurohypophysis, present diagnostic and therapeutic challenges due to their nonspecific imaging features and clinical overlap with other sellar tumors. Our systematic review and meta-analysis summarize radiological, pathological, and surgical outcomes, highlighting the diagnostic utility of advanced imaging and immunohistochemistry, while underscoring the need for tailored surgical strategies to optimize patient outcomes. We emphasize the persistent ambiguity surrounding the biological behavior and prognostic determinants of pituitaryomas, despite advances in imaging and molecular diagnostics. Thus, the integration of immunohistochemical markers with detailed MRI characterization has emerged as a critical strategy for improving diagnostic accuracy in these cases. However, variability in surgical outcomes and recurrence patterns highlights the need for individualized, multidisciplinary approaches and reinforces the importance of long-term surveillance.

The MRI plays a pivotal role in the diagnostic evaluation of pituitaryoma, rare benign tumors originating from pituitary cells in the neurohypophysis, despite the inherent diagnostic challenges posed by their

nonspecific imaging characteristics. MRI's superior soft-tissue contrast and multiplanar capabilities enable precise visualization of the posterior pituitary, where pituitaryomas typically present as well-defined, homogeneous lesions.¹⁹ On conventional MRI sequences, pituitaryomas generally appear isointense on T1-weighted images and hyperintense on T2-weighted sequences, with intense and homogeneous contrast enhancement being a frequently observed feature.²⁰ Post-contrast T1-weighted images frequently demonstrate moderate to intense enhancement due to the tumor's vascularity, though this is not pathognomonic.²¹ In recent years, advanced MRI techniques such as diffusion-weighted imaging and dynamic contrast-enhanced ((DCE-MRI) sequences have been explored to improve tissue characterization, though their diagnostic yield remains under investigation. However, DCE-MRI have demonstrated that pituitaryomas may exhibit earlier and more homogeneous enhancement kinetics compared to adenomas, reflecting their distinct vascular architecture and potentially aiding in differential diagnosis.²² Thus, continued refinement of MRI protocols and incorporation of advanced imaging techniques remain critical to improving diagnostic accuracy and guiding surgical planning in this uncommon neurohypophyseal neoplasm.

The findings of our study, summarized in the sixth column of Table 1, consistently characterize pituitaryomas as sellar or suprasellar masses exhibiting isointense signal intensity on T1-weighted images and hyperintense signal on T2-weighted sequences. Notably, all patients evaluated with [¹⁸F]FET PET/MRI demonstrated positive uptake, underscoring the high sensitivity of this modality for detecting these tumors, even when conventional MRI findings are ambiguous. Such characteristics contribute to the diagnostic challenge, as pituitaryomas share overlapping features with other sellar lesions, including pituitary adenomas and meningiomas. However, the integration of conventional MRI signal patterns with advanced molecular imaging using [¹⁸F]FET PET/MRI enhances preoperative localization and characterization, facilitating more accurate diagnosis and surgical planning.

Immunohistochemical profiling plays a fundamental role in accurate diagnosis. Pituitaryoma is characterized by a distinctive immunohistochemical profile that is instrumental for its diagnosis.²³ Nuclear expression of TTF-1 is universally present and represents the most reliable marker, effectively distinguishing pituitaryoma from other sellar and suprasellar neoplasms.²⁴ S100 protein is also frequently positive, while GFAP demonstrates variable, often focal, positivity, reflecting the tumor's neuroglial origin.^{25,26} Epithelial membrane antigen (EMA) and synaptophysin may show focal or weak staining in a subset of cases, but are not consistently expressed.^{27,28} The Ki-67 proliferation index remains low in non-atypical pituitaryomas, supporting their generally indolent behavior.²⁹ This immunoprofile, particularly the strong and diffuse TTF-1 positivity, is fundamental for accurate diagnosis, especially given the overlapping histological features with other sellar tumors, and collectively facilitate accurate diagnosis, particularly in distinguishing pituitaryoma from other sellar lesions.

Our systematic review and meta-analysis of pituitaryoma incorporated data from four key studies, revealing consistent expression of several immunohistochemical markers. TTF-1 and S100 were recurrently identified across most reports, underscoring their diagnostic significance. GFAP and vimentin

also appeared frequently, reflecting the tumor's glial lineage, while EMA and synaptophysin showed variable positivity, suggesting some phenotypic heterogeneity. Ki-67 proliferation indices were reported in one study, generally indicating low proliferative activity consistent with the tumor's indolent nature. Our findings emphasize the necessity of a comprehensive immunohistochemical panel to accurately characterize pituicytomas and distinguish them from other sellar neoplasms, enhancing diagnostic precision and informing clinical management.

Pituicytomas require meticulous surgical planning to achieve optimal outcomes while preserving pituitary function. Surgical resection remains the definitive treatment for pituicytoma, with GTR strongly associated with favorable prognosis and markedly reduced recurrence rates. However, the tumor's pronounced vascularity and firm adherence to critical neurovascular structures often complicate complete excision, increasing the risk of perioperative morbidity and endocrine dysfunction.³⁰ The GTR when feasible, can be carried out via transsphenoidal or transcranial approach depending on tumor extension and anatomical involvement. Given their location in the sellar region, preservation of surrounding neurovascular structures, particularly the optic apparatus and hypothalamus, is critical to minimize postoperative morbidity.³¹ Endoscopic techniques have increasingly been favored for better visualization and reduced invasiveness.³² However, subtotal resection followed by close radiological monitoring may be considered in cases of extensive adherence to critical structures. Adjuvant therapies, including radiotherapy, remain poorly defined due to the rarity of these tumors, but may be contemplated in cases with aggressive behavior or recurrence.³³ Multidisciplinary decision-making involving neurosurgeons, endocrinologists, and neuropathologists is essential to tailor individualized treatment strategies.

Our study revealed a diverse spectrum of surgical approaches employed in pituicytoma management across the four selected studies. Transsphenoidal and transcranial routes were the predominant modalities, reflecting tumor location and extent, with endoscopic transsphenoidal techniques increasingly favored for their minimally invasive profile. Additionally, stereotactic radiosurgery modalities such as Gamma Knife and CyberKnife were reported as adjunct or alternative treatments, particularly in cases of subtotal resection or recurrence. The choice of approach was consistently tailored to optimize tumor resection while minimizing neurological and endocrine morbidity. This heterogeneity underscores the necessity for individualized surgical planning, balancing maximal safe resection against preservation of pituitary function, and highlights the evolving role of advanced minimally invasive and radiosurgical techniques in managing this rare neurohypophyseal tumor.

Surgical management of pituicytoma presents challenges in endocrine recovery and metabolic outcomes. Despite effective tumor control, persistent or worsened endocrine dysfunction postoperatively is common, underscoring the need for vigilant long-term endocrine follow-up.³⁴ GTR is associated with low recurrence rates and improved long-term control, although subtotal removal is sometimes necessary to preserve critical neurovascular structures.³⁵ Advances in neuroendoscopic techniques have improved visualization and resection completeness, with GTR rates of 75% in pituitary

tumors broadly, with recurrence rates as low as 4.3% following complete excision, and reduced complication rates compared to microscopic surgery.³⁶ Postoperative complications underscoring the need for meticulous surgical technique.³⁷ Recurrence rates, reported at 27.3–36.4% over 5 years, are higher after partial resection, necessitating long-term MRI surveillance.^{11,18,38} These improvements translate into enhanced quality of life and reduced recurrence, though specific data on pituicytoma remain limited. Multidisciplinary care integrating surgical expertise and endocrinological management remains essential to optimize outcomes.

Our results encompassing four selected studies on pituicytoma revealed heterogeneous outcome measures, reflecting the variability of this tumor. While one study did not specify recurrence rates, limiting direct comparisons, others reported a high short-term remission rate of 75%, indicating favorable initial surgical outcomes. However, recurrence and progression remain significant concerns, with reported rates of 27.3% and 36.4% following surgical resection in two separate cohorts. These findings underscore the variability in post-treatment behavior and emphasize the need for long-term follow-up due to the risk of late recurrence or progression, despite seemingly successful initial management.

In summary, this systematic review and meta-analysis provide valuable insights into the clinical complexity of pituicytomas, emphasizing the importance of a multimodal diagnostic and therapeutic approach. The findings reinforce the utility of immunohistochemistry and characteristic MRI patterns in differentiating pituicytomas from other sellar tumors. While GTR remains the most effective treatment, the significant recurrence risk following subtotal removal highlights the need for careful surgical planning and long-term radiological monitoring. Despite the limitations imposed by the rarity of these lesions, this study contributes to a more standardized understanding of pituicytoma biology, aiding in evidence-based decision-making across multidisciplinary teams.

CONCLUSION

Pituicytoma remains diagnostically challenging due to nonspecific imaging and clinical overlap with other sellar neoplasms. This meta-analysis underscores the diagnostic value of TTF-1 immunohistochemistry, supported by MRI features. Advanced imaging modalities such as [¹⁸F]FET PET/MRI may further improve preoperative identification. The moderate heterogeneity across studies, these results advocate for tailored surgical approaches and vigilant long-term follow-up to optimize patient outcomes in pituicytoma management.

Declarations

Conflicts of interest:

None declared.

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Figures

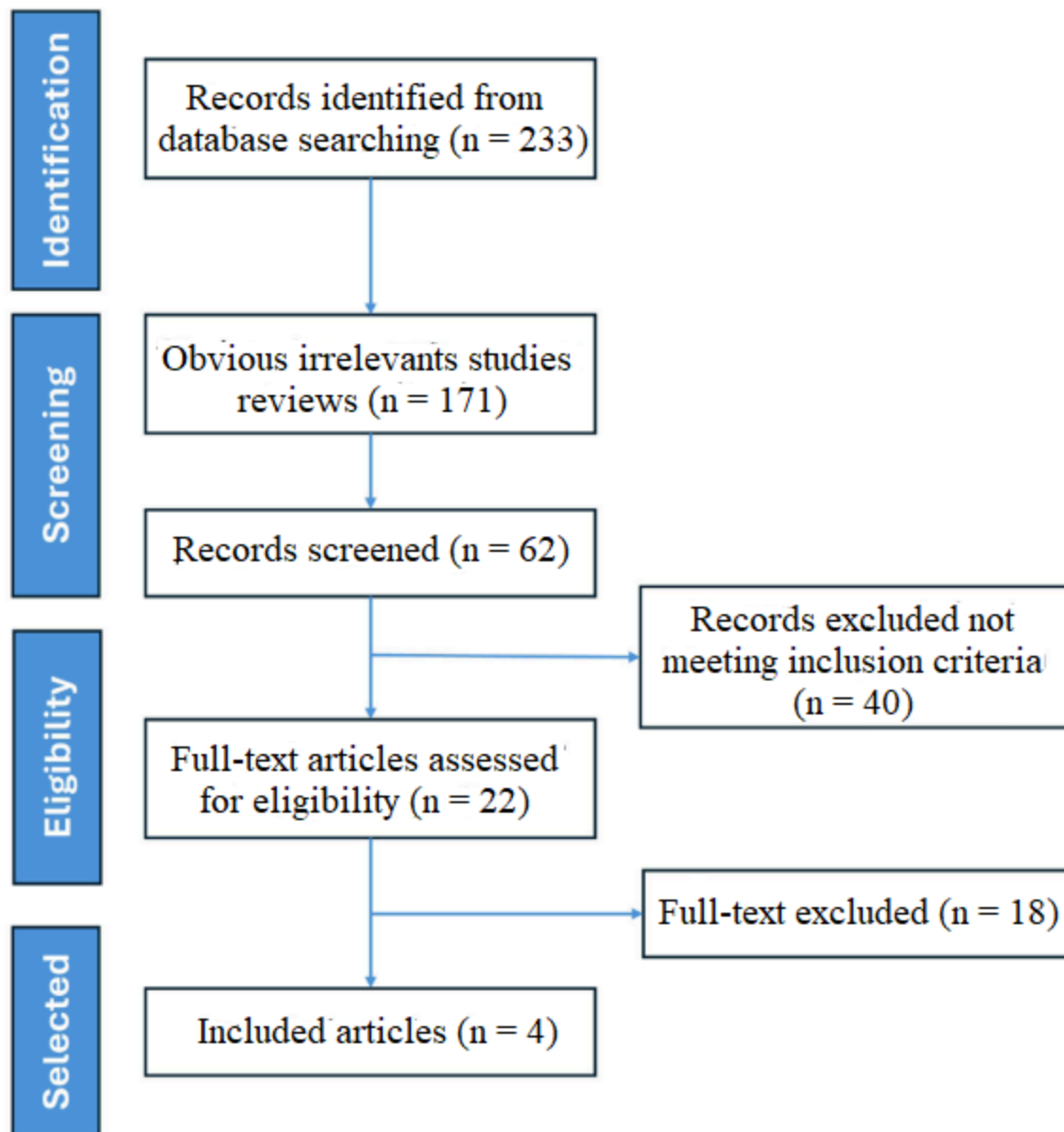


Figure 1

Flowchart of the selection process for the 4 studies included.

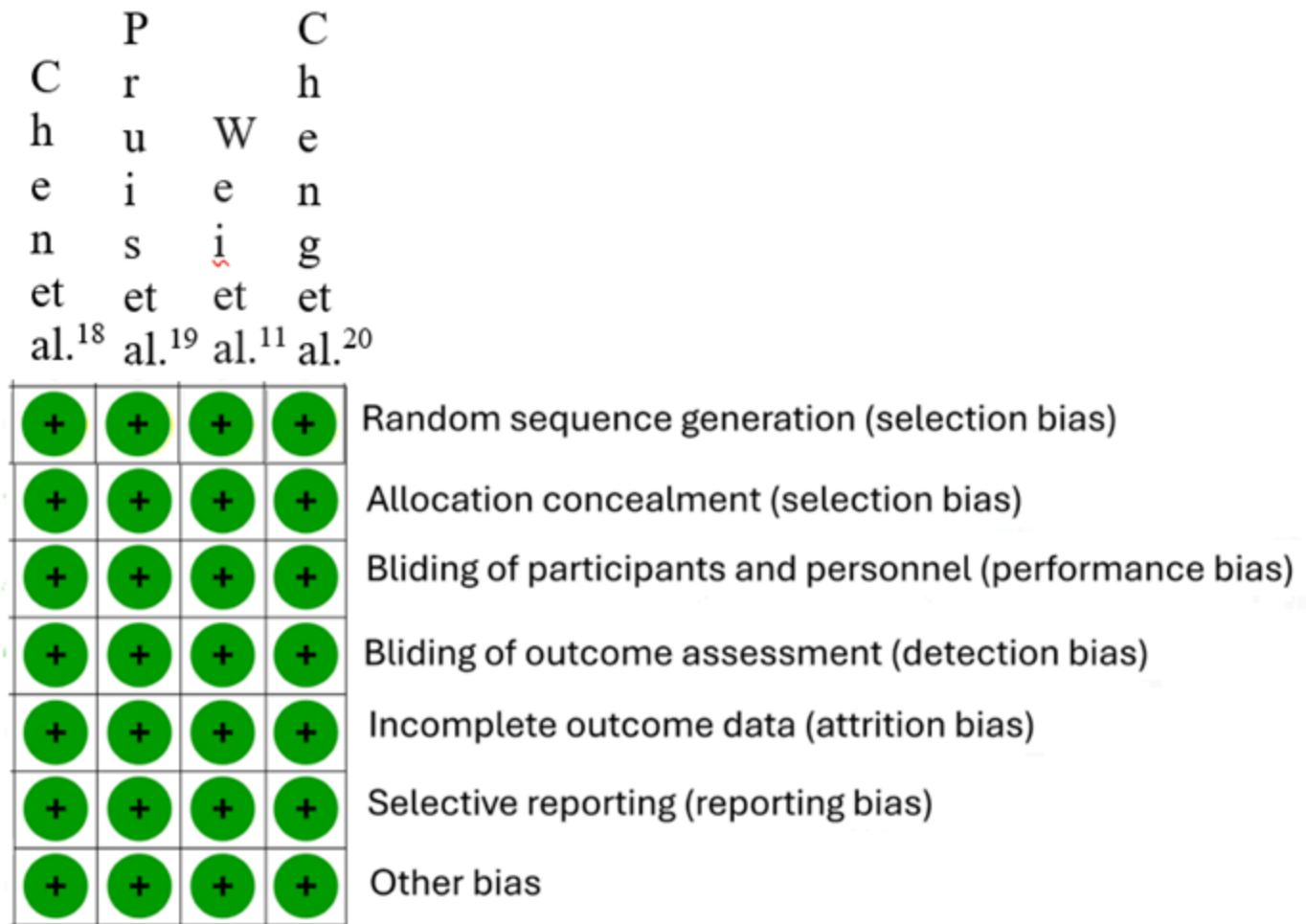


Figure 2

Risk of bias summary.

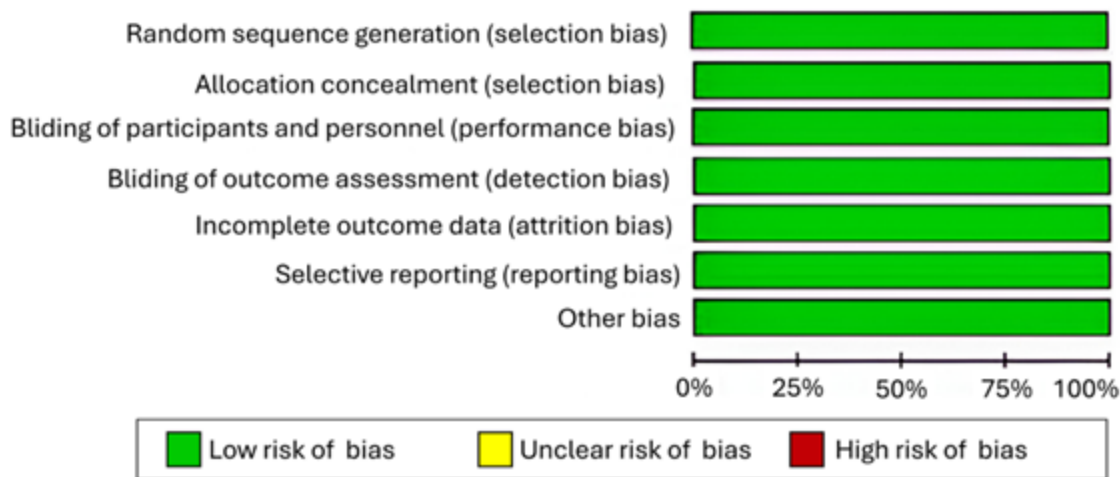


Figure 3

Risk of bias presented as percentage of the included studies

Forest plot

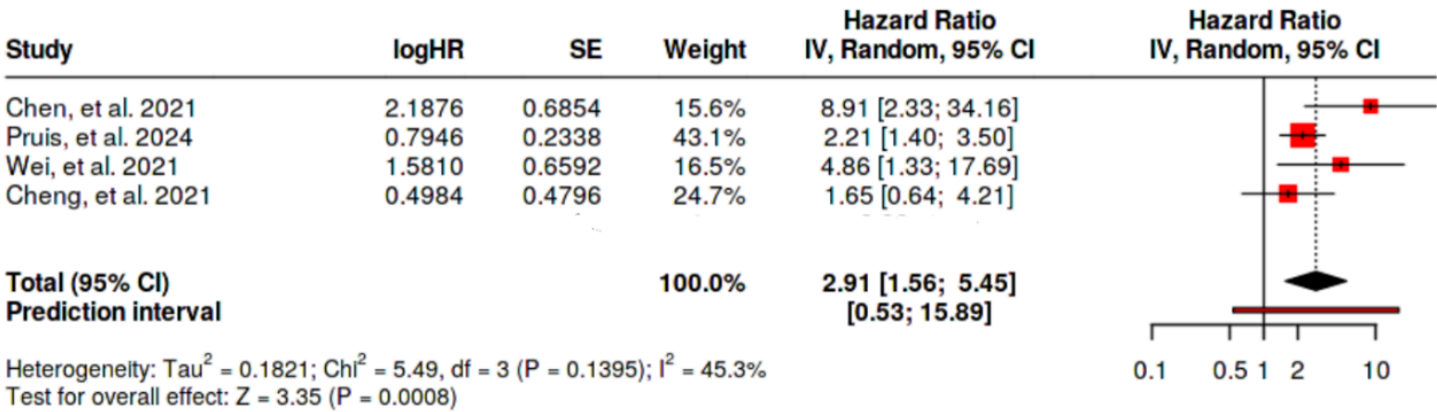


Figure 4

Pituicytoma Cases - Correlating Radiological, Pathological, and Surgical Outcomes in the overall study population.