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Transsphenoidal Surgery for Pituitary Neuroendocrine Tumors (PitNETs) in Elderly versus Younger Patients: A Systematic Review and Meta-Analysis

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ADMINISTRATIVE INFORMATION**Support** - No funding.**Review Stage at time of this submission** - Completed but not published.**Conflicts of interest** - None declared.**INPLASY registration number:** INPLASY202670119

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 29 July 2026 and was last updated on 30 July 2026.

INTRODUCTION

Review question / Objective In patients undergoing transsphenoidal surgery (TSS) for pituitary neuroendocrine tumors (PitNETs), do elderly patients differ from younger patients in surgical, endocrine, and postoperative complication outcomes?

Rationale The effect of advanced age on TSS outcomes for PitNETs remains debated. Previous syntheses reached differing conclusions and predate the 2022 WHO reclassification and recent comparative cohorts. This meta-analysis provides an updated, comprehensive comparison of surgical, endocrine, and systemic outcomes between elderly and younger patients.

Condition being studied Pituitary neuroendocrine tumors (PitNETs) treated with transsphenoidal surgery, focusing on age-related differences in outcomes.

METHODS

Search strategy ("pituitary neuroendocrine tumor" OR "pituitary adenoma" OR "PitNET") AND ("transsphenoidal surgery" OR "endoscopic endonasal surgery") AND ("elderly" OR "older" OR "aged" OR "geriatric") AND ("young" OR "younger" OR "age" OR "comparison" OR "versus").

Participant or population Patients who underwent transsphenoidal surgery for a pituitary neuroendocrine tumor.

Intervention Elderly patients (age threshold as defined by each study: ≥ 65 , ≥ 70 , or ≥ 80 years).

Comparator Younger patients (below the study-specific elderly threshold).

Study designs to be included Comparative observational studies (cohort or case-control).

Eligibility criteria Inclusion: PitNET patients; TSS as primary intervention (endoscopic or

microscopic); comparative elderly-vs-younger outcome data. Exclusion: non-transsphenoidal approaches; fewer than 10 patients in either age group; no direct elderly-vs-younger comparison; case reports, reviews, editorials, letters, or abstracts without extractable data; duplicate cohorts.

Information sources PubMed, Web of Science, Cochrane Library; backward reference screening; author contact by email where needed.

Main outcome(s) Endpoints were grouped into three domains: (1) surgical outcomes, including GTR, postoperative visual improvement, tumor recurrence or regrowth, and reoperation; (2) endocrine outcomes, including permanent and transient diabetes insipidus (DI), postoperative hypopituitarism, and hyponatremia/syndrome of inappropriate antidiuresis (SIADH); and (3) surgical-related and postoperative complications, including intraoperative and postoperative cerebrospinal fluid (CSF) leakage, hematoma or hemorrhage, infection, pneumonia, tumor- or surgery-related mortality, and length of hospital stay.

Additional outcome(s) Study-level variables examined as sources of heterogeneity and used to define prespecified subgroups: surgical technique (pure endoscopic transsphenoidal surgery vs mixed/microscopic), tumor type (nonfunctioning PitNET vs all PitNET subtypes), and the age threshold used to define "elderly" (≥ 65 vs ≥ 70 years). Additional study-level characteristics extracted for descriptive purposes and to assess comparability between groups: country, study period, sample size, sex distribution, tumor size, comorbidity burden (e.g., hypertension, diabetes mellitus, coronary artery disease, Charlson Comorbidity Index, ASA physical-status classification), and length of follow-up.

Data management Records managed in EndNote (RIS); data extracted into a standardized Excel spreadsheet; analyses in R.

Quality assessment / Risk of bias analysis Newcastle–Ottawa Scale (Selection, Comparability, Outcome; total 0–9).

Strategy of data synthesis Random-effects (REML) model when $I^2 > 50\%$, otherwise fixed-effect Mantel–Haenszel; heterogeneity by I^2 . Analyses in R (meta package).

Subgroup analysis Prespecified subgroup analyses were performed according to surgical technique (pure endoscopic), tumor type

(nonfunctioning PitNET), and age threshold (≥ 65 and ≥ 70 years).

Sensitivity analysis Leave-one-out sensitivity analysis; publication bias by funnel plots and Egger's test (≥ 10 studies).

Language restriction English.

Country(ies) involved Japan, Indonesia, and United States.

Keywords pituitary neuroendocrine tumor; transsphenoidal surgery; elderly; younger.

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