

INPLASY PROTOCOL

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Review Stage at time of this submission: Formal screening of search results against eligibility criteria.

Conflicts of interest:
None declared.

Effect of different surgical approaches for papillary thyroid carcinoma of isthmus on postoperative tumor recurrence rate and complications, a systematic review and meta-analysis

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Review question / Objective: The effectiveness and safety of different surgical approaches for papillary thyroid carcinoma of isthmus(PTCI) were evaluated by assessing tumor recurrence, postoperative complications, and prognostic outcomes in patients with PTCI after total thyroidectomy and less-than-total thyroidectomy.

Condition being studied: In 2015, the ATA stated in the treatment guidelines for PTC that total or near-total thyroidectomy is recommended for tumors >4 cm in diameter, cN1, cM1, or the apparent presence of extra thyroidal extension (ETE). For tumor diameter of 1-4 cm, no ETE and no lymph node metastasis, total or near-total thyroidectomy is feasible. However, the scope of surgery and lymph node dissection for PTCI is not clearly defined. Therefore, in clinical practice, there are many controversies among domestic and foreign scholars regarding the scope of surgery for patients with PTCI, and it is difficult to draw credible conclusions due to the low incidence of PTCI and the relatively small number of cases selected from various clinical studies. And there is no relevant meta-analysis, so it is clinically significant to conduct this study.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 24 March 2023 and was last updated on 24 March 2023 (registration number INPLASY202330095).

INTRODUCTION

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METHODS

Search strategy: (((((((((((((((("Thyroid Neoplasms"[Mesh]) OR ("Thyroid Cancer, Papillary"[Mesh])) OR (thyroid carcinoma*[Title/Abstract])) OR (thyroid cancer*[Title/Abstract])) OR (papillary thyroid cancer*[Title/Abstract])) OR (papillary thyroid carcinoma*[Title/Abstract])) OR (papillary thyroid microcarcinoma[Title/Abstract])) OR (thyroid micropapillary carcinoma[Title/Abstract])) OR (papillary thyroid micro carcinoma[Title/Abstract])) OR (thyroid malignancy[Title/Abstract])) OR (dominant malignant nodules[Title/Abstract])) OR (malignant nodules[Title/Abstract])) OR (differentiated thyroid cancer*[Title/Abstract])) OR (Familial Nonmedullary Thyroid Cancer*[Title/Abstract])) OR (Nonmedullary Thyroid Carcinoma*[Title/Abstract])) AND ((isthmus[Title/Abstract]) OR (isthmus[Title/Abstract])) AND (((((((((((("Surgical Procedures, Operative"[Mesh]) OR (Ghost Surgery[Title/Abstract])) OR (isthmusectomy[Title/Abstract])) OR (thyroidectomy[Title/Abstract])) OR (thyroid surgery[Title/

Abstract])) OR (surgical management[Title/Abstract])) OR (General Surgery[Title/Abstract])) OR (surgical[Title/Abstract])) OR (operation[Title/Abstract])) OR (lobectomy[Title/Abstract])).

Participant or population: Differentiated isthmus thyroid cancer (patients who meet the 2015 ATA guidelines criteria for indications for surgical treatment of differentiated thyroid cancer) at the first visit for surgery, regardless of gender and age, all with pathologically confirmed diagnosis.

Intervention: Less than total thyroidectomy, including subtotal thyroidectomy, isthmus plus lobectomy, extended isthmus, and isthmus resection.

Comparator: Total thyroidectomy.

Study designs to be included: Retrospective analysis or randomized controlled trial.

Eligibility criteria: Inclusion criteria(1) The study population in the literature was differentiated isthmus thyroid cancer (patients who met the criteria of the 2015 ATA guidelines for indications for surgical treatment of differentiated thyroid cancer) at the first surgical visit, regardless of gender and age, all with pathologically confirmed diagnosis.(2) The surgical procedures compared in the literature included total thyroidectomy and thyroidectomy with less than total nail excision such as lobectomy plus isthmus and isthmus (including those meeting the above procedures according to the article description of the extent of excision).(3) At least one of the following outcomes should be reported in the included studies: assessment of postoperative laryngeal return nerve injury, postoperative functional recovery, postoperative complications, and oncologic outcomes.(4) Postoperative complications include hypoparathyroidism, laryngeal nerve injury, postoperative bleeding, choking on water, and hypothyroidism.(5) Retrospective studies or prospective studies with >10 cases of trial versus control interventions in the study,

and all studies must have a follow-up time of >2 years. Exclusion criteria (1) The study population included hyperthyroidism combined with thyroid nodules, hyperfunctioning thyroid adenoma, nodular goiter, and other cases of inoperable thyroid cancer according to the 2015 ATA guidelines, secondary surgery, and those with a history of preoperative radiotherapy and other significant organ function changes. (2) The surgical approach was not controlled, although total/subtotal thyroidectomy and lobectomy with isthmus were used, and the surgical approach was different from the above-mentioned procedures, such as the use of lumpectomy. (3) The literature only analyzes and discusses the overall recurrence without comparing the respective recurrence after different surgical procedures in groups; it only analyzes and discusses the overall complications without comparing the respective major complications after different surgical interventions in groups; (4) Repeated studies, case reports, conference abstracts, reviews, letters or syntheses; (5) Studies that included only one intervention; (6) Studies with indicators that are inconsistent with pre-determined indicators; (7) Studies for which the full text was not available. Exclusion criteria (1) The study population included hyperthyroidism combined with thyroid nodules, hyperfunctioning thyroid adenoma, nodular goiter, and other cases of inoperable thyroid cancer according to the 2015 ATA guidelines, secondary surgery, and those with a history of preoperative radiotherapy and other significant organ function changes. (2) The surgical approach was not controlled, although total/subtotal thyroidectomy and lobectomy with isthmus were used, and the surgical approach was different from the above-mentioned procedures, such as the use of lumpectomy. (3) The literature only analyzes and discusses the overall recurrence without comparing the respective recurrence after different surgical procedures in groups; it only analyzes and discusses the overall complications without comparing the respective major complications after different surgical

interventions in groups; (4) Repeated studies, case reports, conference abstracts, reviews, letters or syntheses; (5) Studies that included only one intervention; (6) Studies with indicators that are inconsistent with pre-determined indicators; (7) Studies for which the full text was not available. Exclusion criteria (1) The study population included hyperthyroidism combined with thyroid nodules, hyperfunctioning thyroid adenoma, nodular goiter, and other cases of inoperable thyroid cancer according to the 2015 ATA guidelines, secondary surgery, and those with a history of preoperative radiotherapy and other significant organ function changes. (2) The surgical approach was not controlled, although total/subtotal thyroidectomy and lobectomy with isthmus were used, and the surgical approach was different from the above-mentioned procedures, such as the use of lumpectomy. (3) The literature only analyzes and discusses the overall recurrence without comparing the respective recurrence after different surgical procedures in groups; it only analyzes and discusses the overall complications without comparing the respective major complications after different surgical interventions in groups; (4) Repeated studies, case reports, conference abstracts, reviews, letters or syntheses; (5) Studies that included only one intervention; (6) Studies with indicators that are inconsistent with pre-determined indicators; (7) Studies for which the full text was not available.

Information sources: Pubmed, web of science, Embase, Coherence.

Main outcome(s): The primary outcome of this study is to compare the rate of tumor recurrence in patients with PTCI undergoing total thyroidectomy or less than total thyroidectomy.

Additional outcome(s): The secondary outcome of this study is to compare the incidence of postoperative complications (hypoparathyroidism, nerve damage,

postoperative bleeding, choking on water, etc.) between the two groups.

Quality assessment / Risk of bias analysis:

Since the included studies were retrospective analyses, two authors used the methodological index for non-randomized studies to assess article quality independently. The scale consists of 12 entries, each with a score of 0-2, for a total score of 24. A score of 0 means not reported, 1 means reported but with insufficient information, and 2 means reported and with sufficient information. Disagreements were also resolved through consultation with the third reviewer.

Strategy of data synthesis: Descriptive data were summarized as percentages of categorical data, and continuous data were summarized as mean or median standard deviation (SD) or interquartile range (IQR). Relative risk of tumor recurrence and postoperative complications (risk ratio/RR, 95% confidence interval) was assessed in both groups using a random-effects model.

Subgroup analysis: Subgroup analysis was performed according to tumor TNM stage, patient age, and lymph node dissection.

Sensitivity analysis: Heterogeneity tests were used to determine the degree of heterogeneity across all studies, with 75% being highly variable; sensitivity analyses were performed to explore the impact of study quality and follow-up duration on the risk assessment of tumor recurrence rates and to explore the sources of heterogeneity.

Country(ies) involved: China.

Keywords: Papillary thyroid cancer, isthmus, surgical approach, tumor recurrence rate, complications.

Contributions of each author:

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Author 3 - Anping Su - Author 3 is responsible for the correction of manuscript writing and obtaining financial support.

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