

Comparison between Active Surveillance and Immediate Surgery for Papillary Thyroid Microcarcinoma: Integrative Literature Review

<https://doi.org/10.32635/2176-9745.RBC.2026v72n4.5679EN>

Comparaç o entre Vigil ncia Ativa e Cirurgia Imediata para Microcarcinoma de Tireoide: Revis o Integrativa da Literatura
Comparaci n entre Vigilancia Activa y Cirug a Inmediata en el Microcarcinoma Papilar de Tiroides: Revisi n Integradora de la Literatura

Mariana Filipak Machado¹; Lara Terumi Takayama²; Laura Vivacqua de Barros³; Lucas Kaiser Gomes da Silva⁴; Guilherme Alves Mariath Costa⁵; Theo Kaminski de Souza⁶; Vin cius Basso Preti⁷

ABSTRACT

Introduction: Considering the possibility of diagnosing papillary thyroid microcarcinoma (PTMC) and the low malignant potential in a large proportion of the diagnosed population, introducing active surveillance (AS) as a non-invasive treatment, instead of standard immediate surgery (IS), has been theorized to reduce unnecessary surgeries. **Objective:** To evaluate the different outcomes of immediate surgery and active surveillance strategies for PTMC. **Method:** Twenty-four articles were selected using the PubMed and Embase databases. Screening was performed in a double-blind manner and verified by a third reviewer with the objective of collecting data to conduct a literature review, aiming to compare the outcomes of different strategies. **Results:** Active surveillance was inferred to be more cost-effective than immediate surgery. However, active surveillance showed a higher rate of loss to follow-up, often related to psychological and logistical factors. Survival and quality of life outcomes were inconclusive. **Conclusion:** Active surveillance is shown to be a safe and effective alternative for managing papillary thyroid microcarcinoma and includes several benefits in terms of cost and quality of life, although treatment choice requires an individualized approach. Nevertheless, there is a need for further multicenter and randomized studies to strengthen the evidence base and guide clinical practice.

Key words: Watchful Waiting; Papillary Thyroid Cancer; Cost-Effectiveness; Survival; Quality of Life.

RESUMO

Introdu  o: Com possibilidade do diagn stico de microcarcinoma papil fero de tireoide (PTMC) e o baixo potencial de malignidade em grande parte da popula  o diagnosticada, teoriza-se a possibilidade de introduzir a vigil ncia ativa (VA) como tratamento n o invasivo, ao inv s do padr o preconizado de cirurgia imediata (CI), a fim de diminuir cirurgias desnecess rias. **Objetivo:** Avaliar os diferentes desfechos das estrat gias de CI e VA para PTMC. **M todo:** Foram selecionados 24 artigos utilizando as bases de dados PubMed e Embase. A triagem foi realizada em duplo-an nimo e verificada por um terceiro revisor com o objetivo de coletar dados para a realiza  o de uma revis o de literatura, com o prop sito de comparar os desfechos de diferentes estrat gias. **Resultados:** Inferiu-se que a VA   considerada mais custo-efetiva do que a CI. Por m, a VA possui uma maior taxa de perda de seguimento, frequentemente relacionada a fatores psicol gicos e log sticos. A sobrevida e a qualidade de vida apresentaram resultados inconclusivos. **Conclus o:** A VA se mostra uma segura e eficaz alternativa para o manejo do microcarcinoma papil fero de tireoide, e engloba diversos benef cios em termos de custo e qualidade de vida, embora a escolha do tratamento necessite de uma abordagem individualizada. Por m, destaca-se a necessidade de mais estudos multic ntricos e randomizados para fortalecer a base de evid ncias e guiar a pr tica cl nica.

Palavras-chave: Conduta Expectante; C ncer Papil fero da Tireoide; Custo-Efetividade; Sobrevida; Qualidade de Vida.

RESUMEN

Introducci n: Con la posibilidad del diagn stico de microcarcinoma papilar de tiroides (PTMC) y el bajo potencial de malignidad en una gran parte de la poblaci n diagnosticada, se teoriza la posibilidad de la introducci n de la vigilancia activa (VA) como tratamiento no invasivo, en lugar del est ndar recomendado de cirug a inmediata (CI), con el fin de reducir cirug as innecesarias. **Objetivo:** Evaluar los diferentes desenlaces de las estrategias de cirug a inmediata y vigilancia activa para el PTMC. **M todo:** Se seleccionaron 24 art culos utilizando las bases de datos PubMed y Embase. Se realiz  el proceso de selecci n de forma doble an nimo y fue verificado por un tercer revisor con el objetivo de recolectar datos para la realizaci n de una revisi n de la literatura, con el prop sito de comparar los desenlaces de diferentes estrategias. **Resultados:** Se infiere que la vigilancia activa es considerada mejor costo-efectiva que la cirug a inmediata. Sin embargo, la vigilancia activa presenta una mayor tasa de p rdida de seguimiento, frecuentemente relacionada con factores psicol gicos y log sticos. La supervivencia y la calidad de vida mostraron resultados inconclusos. **Conclusi n:** La vigilancia activa se presenta como una alternativa segura y eficaz para el manejo del microcarcinoma papilar de tiroides e incluye diversos benef cios en t rminos de costo y calidad de vida, aunque la elecci n del tratamiento requiere un enfoque individualizado. No obstante, se destaca la necesidad de m s estudios multic ntricos y aleatorizados para fortalecer la base de evidencias y guiar la pr ctica cl nica.

Palabras clave: Conducta Expectante; C ncer Papilar de Tiroides; Costo-Efectividad; Supervivencia; Calidad de Vida.

^{1,7}Pontif cia Universidade Cat lica do Paran  (PUC-PR). Curitiba (PR), Brasil.

¹E-mail: mariana.filipak@pucpr.edu.br. Orcid iD: <https://orcid.org/0009-0006-3672-685X>

²E-mail: terumilt@gmail.com. Orcid iD: <https://orcid.org/0009-0001-3914-4533>

³E-mail: lauravbarros03@gmail.com. Orcid iD: <https://orcid.org/0009-0003-9228-2489>

⁴E-mail: lucaskaisers@gmail.com. Orcid iD: <https://orcid.org/0009-0009-9681-7448>

⁵E-mail: guilhermemariath@hotmail.com. Orcid iD: <https://orcid.org/0009-0006-5032-6342>

⁶E-mail: theo.kaminski@hotmail.com. Orcid iD: <https://orcid.org/0009-0005-4015-6485>

⁷E-mail: basso.vinicius@pucpr.br. Orcid iD: <https://orcid.org/0000-0002-7574-6611>

Corresponding author: Mariana Filipak Machado. Rua Luiz Ant nio Biazetto, 174 – S o Louren o. Curitiba (PR), Brasil. CEP 82200-050. E-mail: mariana.filipak@pucpr.edu.br



INTRODUCTION

Thyroid cancer incidence has increased significantly, the most prevalent being papillary thyroid cancer (90%)¹. However, this increase is related to the papillary thyroid microcarcinoma (PTMC) diagnosis, a cancer whose maximum diameter is smaller than 1 centimeter and presents extremely low mortality and recurrence risks². Currently, most thyroid cancers are treated with immediate surgery (IS); however, for PTMC, the most up-to-date literature indicates non-invasive treatments as effective alternatives, especially active surveillance (AS)¹.

The main objective of non-invasive management is to reduce patient exposure to surgeries with risks of sequelae and morbidity³. AS is an alternative that began to be acknowledged as a safe treatment strategy in 2015 by the American Thyroid Association, after a comparison between AS and IS demonstrated that, in both strategies, no patient developed distant metastases or died due to the illness¹.

The assessed outcomes include comparisons of psychological impact, vocal cord paralysis, temporary or permanent hypoparathyroidism, and tumor evolution, with emphasis on regional lymph node involvement (N), according to the TNM classification system⁴.

Considering the sample of studies related to this comparison between two treatment strategies for PTMC, summarizing the subject in a review is important to achieve more precise results.

METHOD

Integrative review of articles published over the past ten years to assess the comparison between AS and IS in patients diagnosed with PTMC, analyzing differences in cost, survival, tumor evolution, loss to follow-up, and complications associated with the surgical procedure.

The review was conducted using the PubMed and Embase databases. The initial search strategy used Boolean tools from the aforementioned databases. The keywords tied to the utilized search in both PubMed and Embase, were, respectively ("papillary thyroid microcarcinoma" OR "carcinoma, papillary" [MeSH Terms] OR "Papillary microcarcinomas" OR PMC OR PMCs) AND ("watching waiting" OR "active surveillance") AND ("Immediate treatment" OR therapeutics [MeSH Terms] OR treatment OR "First treatment") and ('papillary thyroid microcarcinoma'/exp OR 'papillary thyroid microcarcinoma' OR 'carcinoma, papillary'/exp OR 'carcinoma, papillary' OR 'papillary microcarcinomas' OR pmc OR pmcs) AND ('watching waiting' OR 'active surveillance'/exp OR 'active surveillance') AND

('immediate treatment' OR 'therapeutics'/exp OR therapeutics OR 'treatment'/exp OR treatment OR 'first treatment').

Articles with similar titles and abstracts were organized on the *Rayyan*⁵ software, version 1.4.3, and analyzed by two independent reviewers to screen for duplicates. After selection based on the duplicate screening search strategy, a double-anonymized screening of titles and abstracts was conducted by two independent reviewers. After the double-anonymized screening, the third researcher was included to discuss and select articles that diverged between the first two researchers.

The inclusion criteria defined for this review were: observational articles of randomized clinical trials, with the population assessed being diagnosed with PTMC, comparing two intervention methods — IS and AS.

The exclusion criteria were established as studies with a review design or that did not make full access available in the selected databases.

The eligible works were read independently by 7 authors who summarized the topics addressed, grouped into 5 relevant topics: cost comparison, survival comparison; quality of life comparison; tumor evolution comparison; and loss to follow-up. Data extraction was grouped in an Excel spreadsheet, divided into columns for articles and lines for each data point (year of publication, population, outcomes, biases, and subgroup analyses).

The risk of bias assessment of the included studies was conducted according to the methodological design of each study, following the selection of appropriate methodological quality assessment instruments. Validated tools used in literature for each type of study design were employed⁶⁻⁹.

The cohort studies were assessed using the Risk of Bias In Non-randomized Studies of Interventions (ROBINS-I V2) tool⁹. For economic studies, Drummond's checklist was used⁷. Cross-sectional studies were assessed using the JBI Critical Appraisal Checklist for Analytical Cross-Sectional Studies⁶, while qualitative studies were analyzed using the JBI Critical Appraisal Checklist for Qualitative Research⁸.

The risk of bias assessment was conducted independently by two reviewers. Occasional disagreements were solved by consensus and, when needed, by consulting a third reviewer. The assessment results were presented descriptively, considering the specific domains of each instrument (Figure 1).

RESULTS

The initial search identified 232 articles in PubMed and 410 in Embase, totaling 642 articles. After removing

duplicate articles, the sample totaled 430 articles. For full reading, 87 articles were selected.

After this selection, during full reading, 41 articles were discarded for not meeting the inclusion criteria, and 22 were discarded for not making full reading available. The 24 remaining articles were considered adequate and relevant, read in full for data extraction and detailed analysis.

When analyzing the articles, a predominance of prospective and retrospective cohorts was observed in the

assessment of results between AS and IS for the treatment of PTMC with different objectives of comparing them with costs and survival, for instance. In total, there were more than 10 prospective studies^{4,11-22}, demonstrating a greater focus on data analysis for future follow-up.

The relevance of the theme is underscored by the growing number of recent publications, with most articles analyzed having been published in 2020. It was also observed that, of all the analyzed articles, more than 10 are from Asia, from countries such as Korea, Japan,

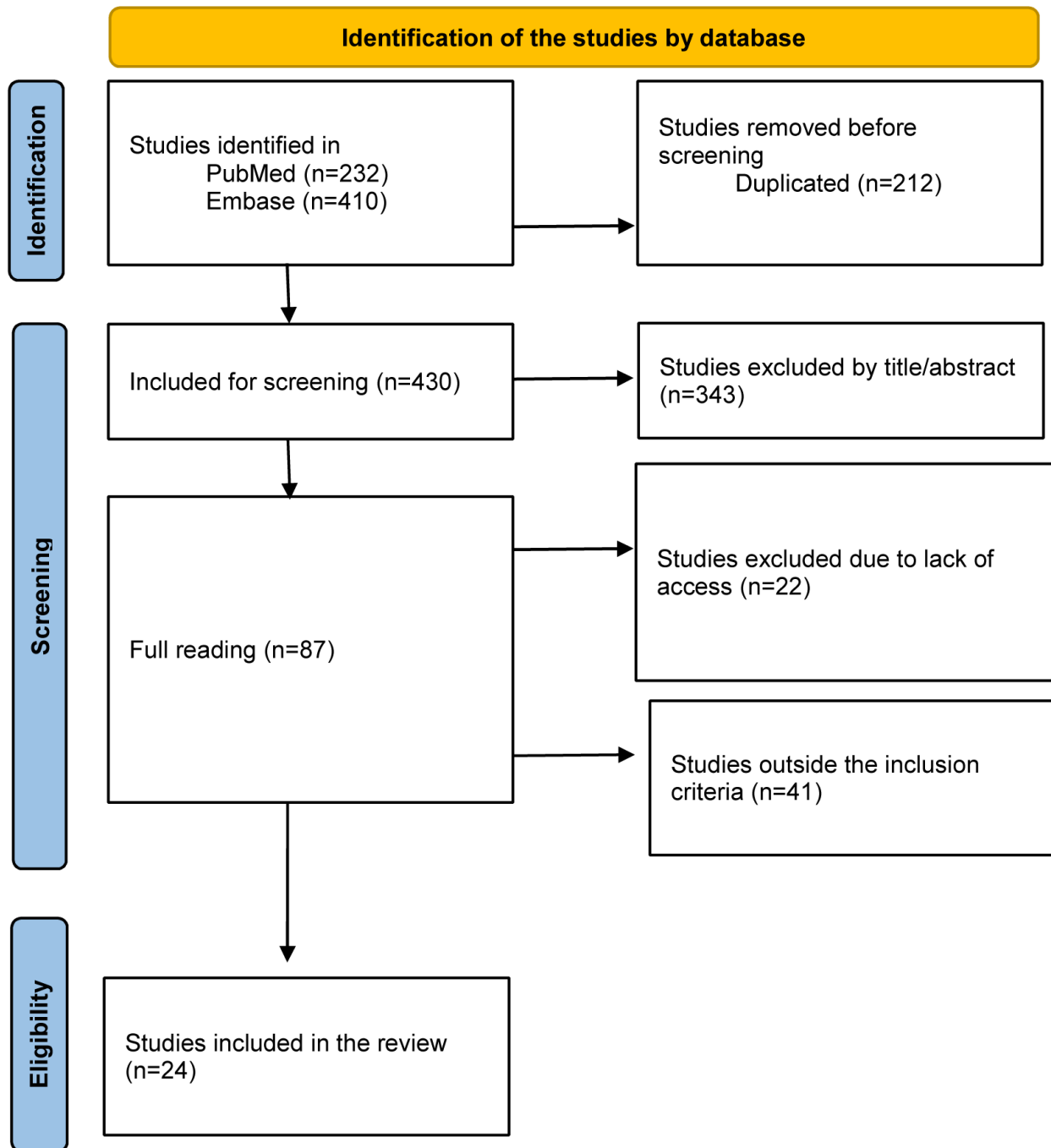


Figure 1. Flowchart of studies screening and selection

Source: Adapted from Page MJ et al.¹⁰



and China, due to the high incidence of thyroid cancer in that region^{2,3,12,13,15,17,18,22-26}. Despite the high incidence in Asia, there are also relevant studies in America: Brazil, Argentina, United States, and Canada^{1,4,11,19-21,27-30}.

Of the included studies, 13 were classified as presenting a general severe risk of bias according to the ROBINS-I V2 tool⁸. The domain that most contributed to this classification was the confounding bias, identified in 12 studies (Supplementary Figure 1)^{1,4,12-15,17-19,26,27,30}.

In the domain of intervention classification, only two studies presented a severe risk of bias^{27,30}. Regarding participant selection bias, three studies were classified as severe risk^{1,27,30}. Regarding the absent data domain, studies by Griffin et al. and Lin et al. presented a severe risk of bias. In the measurement of outcomes domain, three studies were classified as severe risk^{13,17,25}. On the other hand, no study presented a severe risk of bias in the reported result selection domain.

In the overall judgment by ROBINS-I V2⁹, four studies were classified as presenting a moderate risk of bias. Among them, the study by Sawka et al.¹¹ received this classification due to confounding bias and participant selection domains. Whereas the study by Sawka et al.²⁰ was classified as moderate risk due to the domains of confounding bias, participant selection, and measurement of outcomes. The study by Saito et al.²⁵ presented a moderate risk due to the domains of confounding bias, absent data, and reported result selection. Finally, the work by Sawka et al.²¹ was classified as moderate risk exclusively due to the confounding bias (Supplementary Figure 1).

According to Drummond's checklist⁷, the study by Lai et al.²⁴ presented a positive assessment in all domains, with no negative judgment. In contrast, the work by Faro et al.²⁹ received a partial classification in the item referring to the adjustment for incremental analysis and a negative classification regarding the adjustment for time horizon differences (Supplementary Figure 2).

Regarding the risk of bias assessment using the JBI instrument for cross-sectional studies⁵, three studies presented a negative judgment in the domain referring to confounding factors control strategies^{2,22,23}. In the domain related to valid and reliable measurement of outcomes, the works by Yoshida et al.³, Sugitani et al.²², and Nakamura et al.²³ received an uncertain classification (Supplementary Figure 3).

According to the JBI checklist for qualitative studies, the study by D'Agostino et al.²⁸ presented a positive judgment in all assessed domains, with no methodological limitations identified according to the instrument's criteria (Supplementary Figure 4).

The main findings of the included studies are presented in Table 1, enabling an overall view of the main observed results.

DISCUSSION

This integrative review demonstrates that AS constitutes a consistent therapeutic strategy for carefully selected patients with low-risk PTMC. Low rates of tumoral progression, recurrence, and mortality related to the disease were observed, regardless of the initially adopted strategy. However, AS presented advantages related to the reduction of surgical complications and assistant costs, while IS remained associated with the definitive neoplasm treatment, reducing the need for prolonged monitoring.

The literature presents methodological limitations that impair more precise, direct comparisons between the two approaches, such as lack of randomization, geographic variability, and discrepancies in the analyses of quality of life. In this context, further studies will have to include more diversified samples, higher control of confounding factors, and better quality of life analysis to produce more robust evidence for clinical decision-making.

In a prospective cohort study that participated in the Multicenter Prospective Cohort Study of Active Surveillance on Papillary Thyroid Microcarcinoma (MAeSTro), 203 patients in AS and 192 in IS were compared regarding costs, with no significant difference in the perception of patients regarding cost ($p=0.845$)¹³.

Unlike the previous study, the Chinese work assessed the relation between 242,928 Chinese yuans and lifetime-adjusted quality of life, for which it was demonstrated that AS, in general, was a more cost-effective approach for PTMC than IS in different age groups, even though in younger ages surgery can be more cost-effective²⁴.

In agreement with that result, a retrospective cohort study in Australia hypothesized the pairing between AS and surgery. Due to AS not being actively offered for low-risk PTMC at the Royal North Shore Hospital in Sydney, the data were therefore based on the American Thyroid Association Guideline 2015 *vs.* a hypothetical AS. As an outcome, it was concluded that the cost of surgery equaled 16.2 years of AS. Regarding the younger group, more specifically, aged 20 to 30 years, AS exceeded the cost of IS after eight years of follow-up, while for patients aged 70 to 80 years, the cost of surveillance exceeded the cost of surgery after 16.5 years²⁵.

However, when analyzing different AS follow-up intervals, such as biannual or annual, the cost decreased, overcoming that of surgery only after 45.1 years. This demonstrated that for patients in the Australian context who need AS follow-up for longer than 16.2 years, surgical treatment could be considered²⁵.

Another cohort study at Kuma Hospital, in Japan, compared patients with low-risk PTMC submitted to

Table 1. Main findings from articles

Article	Costs	Survival	Quality of life	Tumor evolution	Loss to follow-up	Other complications
Griffin et al. ¹	NI	NI	NI	NI	NI	Appropriate, Nodules <1 cm – Temporary hypoparathyroidism: 3; Ideal, Nodules between 1.1 cm and 1.5 cm – Temporary hypoparathyroidism: 5 – Permanent vocal cord paralysis: 1; Appropriate, Nodules between 1.1 cm and 1.5 cm: – Permanent hypoparathyroidism: 1 – Temporary vocal cord paralysis: 1 – Vocal cords edema: 1
Jeon et al. ²	NI	NI	AS: better QL, greater loss of sexual interest, similar to anxiety about disease progression	NI	NI	NI
Yoshida et al. ³	NI	NI	AS group – Greater anxiety level	NI	NI	NI
Smulever and Pitoia ⁴	NI	NI	NI	Of the 41 patients initially submitted to AS, 12 underwent surgery due to: – Anxiety about disease progression: 8 – Tumor progression: 2 – Lymph node metastasis: 1. Of the 123 patients who underwent IS, evolved: – Tumor progression: 84 – Lymph node recurrence: 2	NI	Hypoparathyroidism: 17% – Transitory hypoparathyroidism: 9.6% – Partial hypoparathyroidism: 2.2% – Permanent hypoparathyroidism: 5.1%. Lesions of the recurrent laryngeal nerve: 2.9% – Transitory RLN lesion: 0.7% – Unilateral paralysis: 1.5%. Local complications: 4.4%. (Hematoma (1.4%), surgical site infection (0.7%), and keloid (2.2%))
Sawka et al. ¹¹	NI	NI	NI	NI	NI	Population factors related to the choice of AS: Advanced age; Lower education level; and Surgeon outside research institutions
Oda et al. ¹²	NI	No related deaths	NI	Of the 91 AS submitted to surgery: – Individual decision: 51 – Tumor progression: 27 – Metastasis: 6 – Undeclared: 6. Recurrence (IS): 5 patients – Contralateral lobe – Metastasis: 3	Deaths due to other causes — IS group: 3 patients; AS group: 5 patients	IS: more vocal paralysis, temporary and permanent hypoparathyroidism, use of levothyroxine
Kong et al. ¹³	Perception of patients similar between AS and IS	NI	AS: better physical and psychological health	Recurrence (IS): 0; Tumor progression: 1	Unspecified (n=4); Anxiety about disease progression (n=3); Non-progressive lymph node finding (n=1)	Hypothyroidism (16.2%) Voice alteration (8.3%) Local hematomas (1.6%)
Miyauchi et al. ¹⁴	IS = 4.1× cost of 10 years AS	No related deaths	NI	AS group 0.04% higher grade of malignancy needing surgical conversion. IS: fewer recurrence. Extrathyroidal extension: AS<IS. PTMC recurrence: AS>IS. Lymph node recurrence: AS > IS	AS: lower loss pre-covid; IS: lower post-covid	NI

To be continued



Table 1. Continuation

Article	Costs	Survival	Quality of life	Tumor evolution	Loss to follow-up	Other complications
Miyauchi ¹⁵	IS = 4.1× AS	No related deaths	NI	10-year follow-up: – Tumoral increase ≥ 3 mm: 8% – New lymph node metastasis: 3.8%	NI	Greater adverse events in the IS group in comparison with AS: Temporary vocal fold paralysis: 4.1% vs. 0.6%; Temporary hypoparathyroidism: 16.7% vs. 2.8%; permanent: 1.6% vs. 0.08%
Molinaro et al. ¹⁶	NI	NI	NI	AS group tumor progression: 3%. 93 participants in AS submitted to surgery due to: – Individual decision: 20% – Tumor evolution: 3%	NI	NI
Moon et al. ¹⁷	NI	NI	AS: better QL (physical, psychological, and social)	101 patients migrated from AS to surgery, 35 due to objective progression	Loss to follow-up (AS): 57	NI
Oda et al. ¹⁸	IS = 4.7–6.5× AS	NI	NI	Recurrence: IS 0.51%; AS 0.08%	Deaths due to other causes IS Group: 5 patients AS Group: 3 patients	Permanent hypoparathyroidism: TT 4%; PT 0%. Levothyroxine: TT 100%; PT 42.6%; AS 16.2%
Rosario et al. ¹⁹	NI	NI	AS accepted by 80%	In 30 months, only 1 patient presented with tumor progression, solved through surgery. Since only 1 patient presented with progression, it was not possible to analyze predictors for this variable. A total of 3 patients experienced a reduction in tumor volume of more than 50%	NI	NI
Sawka et al. ²⁰	NI	NI	AS Group – Level of satisfaction with the decision: 98%	NI	NI	NI
Sawka et al. ²¹	NI	NI	AS: better psychological health	NI	Unrelated death (AS): 1 Loss to follow-up (IS): 4	NI
Sugitani et al. ²²	AS<IS	NI	NI	NI	NI	NI
Nakamura et al. ²³	NI	NI	IS: more complaints related to voice, psychological health, problems with scarring, and weight gain	NI	NI	IS: temporary vocal cords paralysis (6%), temporary hypoparathyroidism (33%), permanent hypoparathyroidism (4%)
Lai et al. ²⁴	AS more cost-effective (242,928 yuans/QALY)	NI	QALY AS had better scores	NI	NI	NI
Saito et al. ²⁵	NI	NI	NI	Of the 227 AS participants, 19 converted to surgery due to: – Tumoral progression, emergency related to another disease, Graves' disease, and change of doctor	Loss to follow-up: (AS>IS), peak between diagnosis and 2-year window – Death due to other causes: 0. Gender, distance to the hospital, and method of diagnosis had no association with loss to follow-up	NI

To be continued

Table 1. Continuation

Article	Costs	Survival	Quality of life	Tumor evolution	Loss to follow-up	Other complications
Sasaki et al. ²⁶	NI	NI	NI	No deaths from cancer; no distant metastases. Recurrences (AS group) – Lateral lymph nodes: 1. Recurrences (IS group) – Neck: 9 – Thyroid: 6 – Lateral lymph nodes: 3	NI	IS: more postoperative hematoma, transitory/persistent hypoparathyroidism, and vocal cords paralysis
Lin et al. ²⁷	IS = 16.2 years (biannual AS) or 45.1 years (annual AS)	Adjuvant RAI did not increase disease-free survival	NI	OP group with recurrent disease: distant metastasis 17%; OP group without recurrent disease: lymph node recurrence 14%	NI	TT: Temporary hypokalemia (n=17); Permanent hypoparathyroidism (n=8); Laryngeal nerve lesion (n=1). Hemithyroidectomy: Permanent Hypothyroidism (n=4); Local hematomas (n=3); Chyle leak (n=1)
D'Agostino et al. ²⁸	NI	NI	IS Group: – decision for treatment due to fear of AS and stigma of cancer diagnosis. AS Group: – perception of PTMC as non-fatal and not needing invasive treatment	NI	NI	Perception of patients on AS: fear due to vulnerability to progression and intense anxiety
Faro et al. ²⁹	AS<PT<TT (502.96; 591.17; 1,180.42); Values do not consider medication costs	NI	NI	NI	NI	NI
Smulever and Pitoia ³⁰	NI	NI	NI	Tumor progression (AS): 26% – Increase ≥3 mm: 17% – Reduction ≥3 mm: 9%. A total of 10 participants switched from AS to surgery due to: – Tumor progression: 2 – Individual decision: 8	Loss due to anxiety given disease progression (AS): 10%	NI

Captions: AS = active surveillance; IS = immediate surgery; OP = operation; QL = quality of life; PTMC = papillary thyroid microcarcinoma; QALY = quality-adjusted life years; TT = total thyroidectomy; PT= partial thyroidectomy; RAI = radioactive iodine; DFS = disease-free survival; NI = not informed.

IS (1,235 people) or AS (974 people), with semiannual or annual ultrasound follow-up. Surgery, including procedures and the postoperative period, costs 4.1 times more than AS over a 22-year follow-up period¹³. In a later analysis with a 30-year follow-up and the same profile of patients, no significant differences were observed. AS has been demonstrated to be an option for treating initial low-risk PTMC when analyzing cost-effectiveness¹².

In another cohort study conducted at the same hospital, with a population likely similar to that of Miyauchi et al.¹⁵, the cost analysis with the use of an assessment model in steps demonstrated similar results. In ten years of follow-up, it was observed that the cost of IS was 4.1 times higher than that of AS, following the same pattern from the previous study¹⁸.

In Brazil, within the SUS treatment context, the total cost results for AS were lower than those of patients who

underwent total (TT) or partial thyroidectomy within 30 years. AS cost 502.96 dollars in that period. In comparison with the same period, partial thyroidectomy cost 591.17 dollars and TT cost 1,180.42 dollars³⁰.

In Japan, a questionnaire applied in 134 institutions assessed the management of nodules smaller than/equal to 10 mm suspicious of malignancy on the ultrasound, with no extrathyroidal involvement. AS presented a lower cost than IS. In four of those institutions, an AS management rate was even proposed to compensate for the difference between the two treatments²².

In general, AS presented better cost-effectiveness than IS in low-risk PTMC. It is important to highlight, however, that patients' age may influence this comparison, as younger patients tend to follow up for longer periods. Furthermore, both the costs of IS and AS also presented variations according to the country where patients are treated.



Different outcomes on survival were observed, exposing different perspectives and analyses on the theme discussed. In a retrospective cohort study, 349 patients who opted for IS were assessed. Disease-free survival (DFS), overall survival (OS), and specific five-year disease survival were 94.5%, 97%, and 100%, respectively²⁷.

Recurrence was diagnosed in 11 patients (3.2%). Most patients with recurrence presented new distant metastases ($n=6$; 1.7%); the remaining had recurrence in locoregional lymph nodes ($n=5$; 1.4%). All 11 patients with recurrence went through previous lymph node dissection, with 9 presenting postoperative lymph node positivity. Postoperative Radioactive Iodine (RAI) was used for all 9 patients with positive lymph nodes 1 month after surgery. The mean time to recurrence was 14.3 months. Adjuvant RAI did not increase DFS ($p=0.104$). Finally, the univariate analysis identified lymph node positivity and extrathyroidal extension as factors associated with papillary thyroid carcinoma recurrence ($p<0.009$ in both cases). Such analysis did not indicate an association between recurrence and factors like age, sex, tumor size, lymph node involvement, extrathyroidal extension, venous invasion, multifocality, or adjuvant RAI. This study, however, did not compare patients who opted for IS with another population, as its objective was to analyze the outcomes of the group based on a hypothetical value for those who would choose AS²⁷.

The studies analyzed present survival data of patients with papillary thyroid carcinoma who underwent AS or IS. Although some studies exclusively include microcarcinomas (tumors ≤ 10 mm)^{3,12,13,17,18,23-30}, others encompass bigger lesions^{1,4,11,20,21,30}, which may influence results related to recurrence and the need for additional therapies, such as adjuvant RAI. These analyses are relevant and deserve discussion, as they contribute to understanding factors that impact patient survival and help in choosing the most appropriate management strategy.

Several review studies investigate the outcomes related to quality of life, comparing AS with IS in issues like physical, mental, and spiritual well-being.

In a prospective cohort study conducted with 203 participants who chose AS and 192 participants who opted for IS, a questionnaire was applied at two different times, upon diagnosis and 8 months after management, in which the patients who opted for AS presented better physical and psychological health in general, being more active in daily activities. Additionally, they presented fewer changes in appetite, fatigue, pain, difficulty swallowing, and voice alterations. However, there was no difference between the groups in factors such as anxiety related to the diagnosis, depression, recurrences, and metastases¹³.

In another prospective cohort study, patients were divided into 674 using AS as treatment and 381 using IS. Then, they responded to a questionnaire that addressed four dimensions of quality of life — physical, psychological, spiritual, and social — in which overall health is calculated by the mean of these dimensions. As a result, there was a higher quality of life score in the AS group in relation to physical, psychological, and social aspects compared to the group that chose surgery. Moreover, a higher score in physical and social health was reported by patients who underwent lobectomy/isthmectomy (L/I) compared with those who underwent TT. Therefore, the quality-of-life relationship in the general aspect was demonstrated as ($AS>L/I>TT$), with advanced age and male sex being the factors most associated with a higher score¹⁷.

In that same sense, another cross-sectional study conducted in Japan, with 298 patients who underwent AS and 49 who chose IS, reported a higher number of psychological complaints, voice issues, weight gain, and problems with scarring in the IS group, in addition to anxiety and depression complaints reported through the Hospital Anxiety and Depression Scale (HADS), in which the mean score for the AS group was 6 and the IS group, 8, showing a significant difference²³.

And yet, in more than one prospective cohort study focused on regretting the decision afterwards and fear of disease progression, with 151 patients who opted for AS and 40 who chose IS, it was inferred that there was no significant difference in the level of decision regret for patients who chose AS or IS. However, the level of decision regret was significantly higher in patients who switched from AS treatment to surgery, when compared to those who performed IS or remained in AS. Furthermore, the fear of disease progression questionnaire, when applied at the beginning of the treatment, indicated greater fear in those interviewed in the surgery group; however, the follow-up survey one year later showed no significant differences between the groups²¹.

A cross-sectional study with 191 patients, including 148 who underwent IS and 43 under AS, observed that the surgery group reported more issues, including neuromuscular symptoms (coef: 4.99 [IS 0.63–10.62], $p=0.020$), discomforts in the throat/mouth (coef: 5.28 [IS 0.18–10.38], $p=0.043$), and dissatisfaction with the scar (coef: 9.34 [IS 4.38– 14.29], $p<0.001$). On the other hand, patients in AS reported greater loss of interest in sexual activities. However, there was no significant difference regarding disease progression-based anxiety between the two groups. This study also compared parameter differences between open and robotic surgeries: no significant differences were demonstrated regarding quality of life².

In conclusion, by analyzing the different articles, it is possible to infer that there is no ideal management method when focusing on quality of life, comparing IS with AS. While some studies report better quality of life for patients in the AS treatment group, others report no significant difference between the groups.

A study conducted in Australia, in which 349 patients with PTMC underwent IS, most patients with recurrent disease presented new distant metastases ($n=6$; 1.7%) and the others presented locoregional recurrence in lymph nodes ($n=5$; 1.4%). All 11 patients who presented with recurrences had undergone positive lymph node dissection after surgery. It is worth highlighting that multivariate analysis did not indicate an association between recurrence, age, sex, tumor size, lymph node involvement, extrathyroidal extension, venous invasion, multifocality, or adjuvant RAI²⁷.

Another study conducted in Japan observed tumor evolution in pregnant patients. Considering this analysis, 8% of the 51 patients who got pregnant during the study presented a tumor increase during pregnancy. All the surgeries performed after delivery were successful. Regarding non-pregnant patients who chose AS, 1,082 of the 1,235 patients did not present disease evolution during observation. In the initial results of these same patients, less than 10% presented with a tumor increase greater than 3 mm, 1% had metastases, and none of the patients who went to surgery after observation presented recurrences¹⁵.

In a later study of the same population, it was observed that patients who chose AS were older at the time of diagnosis and, therefore, had smaller and less multifocal tumors, although more associated with Hashimoto's disease. Of the AS population ($n=3,222$), 12.2% had to undergo conversion surgery for different reasons. However, it is worth mentioning that among patients who underwent conversion surgery, there was no significant difference between patients' age and sex; however, the size of the main tumor was 1 mm larger than in the group who chose surgery in the first moment¹⁴.

In Italy, a study with 185 patients recorded disease evolution in only 3% of the 93 patients who opted for AS in an average follow-up time of 19 months. The patients who chose IS presented excellent surgical results in the short-term follow-up¹⁶. Similarly, a study in South Korea with 395 patients also obtained a satisfactory surgical result, since none of the patients who underwent IS presented disease recurrence after the surgery in the short-term follow-up¹³.

A study conducted in Japan with 1,779 patients followed up in AS compared to 974 submitted to IS observed a higher recurrence rate in the surgery group.

Among the operated patients, 5 presented with disease recurrence after the procedure¹⁸. In another study, conducted by the same authors and using the same cohort of patients in AS, it was reported that 94 of them underwent conversion surgery throughout the follow-up. Among them, the main reason for conversion was patient preference ($n=51$). However, surgery was also performed due to evidence of tumoral increase higher than or equal to 3 mm ($n=27$) or evidence of metastasis in nodal lymph nodes ($n=6$). Of all the patients who underwent conversion surgery, 1 presented with tumor recurrence in the lateral neck compartment¹⁸.

In another study, after the 30-month follow-up of 77 patients submitted to AS, only 1 presented tumor progression and, later, underwent the surgery. It was not possible to analyze predictors of progression due to the low number of events. However, 3 patients of the initial AS total presented a reduction of over 50% of the initial tumor size¹⁹.

Another study conducted in Japan affirms that no patients initially submitted to AS or IS presented distant metastases nor died due to thyroid carcinoma²⁶. This was also observed in a previously mentioned study, in which 5 of the 974 patients who underwent surgery presented recurrence; however, none of them had distant metastases or died¹⁸. Still in the study by Sasaki et al.²⁶, only 1 patient (0.03%) in the AS group presented recurrence of lateral lymph nodes due to tumor size increase. Of the IS patients, recurrence occurred in the neck in 9 patients (0.5%), in the rest of the thyroid in 6 patients (0.3%), and in the lateral lymph nodes in 3 patients (0.2%)²⁶.

In a South American context, in Argentina, 34 of the 136 patients underwent AS. In those, a tumoral growth of 3 mm or larger was observed in 17% ($n=6$), no significant change in size was observed in 74% ($n=25$), and a size reduction of 3 mm or more occurred in 9% ($n=3$). Of the 10 patients who switched to surgery, only 2 did so due to tumoral increase³⁰.

Still in Argentina, another study with a similar sample suggested that only 4.8% ($n=2$) of the 41 patients initially submitted to AS had to undergo surgery due to a tumoral increase of 3 mm or more. In addition to those, 2.4% ($n=1$) of the patients presented with lymph node metastases, which forced them to undergo surgery. On the other hand, of the 123 patients submitted to IS, only 2 developed lymph node recurrence — in the lateral neck compartment⁴.

The percentage of patients who presented tumoral growth is low, regardless of the initially chosen treatment method. In addition, among patients who presented with tumoral growth and/or lymph node involvement, the lateral neck compartment was the most affected. Finally,

it was observed that the choice of initial treatment varies across different world regions, reflecting differences in protocols and clinical approaches, although the tumoral evolution outcomes remain generally favorable in both strategies.

The most reported causes of loss to follow-up were unrelated death^{4,11,18}, emergency due to other related disease, treatment discontinuity (follow-up gap longer than 6 months), change of doctor responsible for follow-up, patient decision, or change of treatment strategy due to tumor evolution^{13,25}. In that last scenario, several studies assessed disease progression in patients initially submitted to the expectant conduct who, given the evolution, migrated to surgical treatment. In the study by Kong et al.¹³, only 1 patient (0.49%) progressed with lymph node metastasis and underwent surgery. Similarly, Molinaro et al. reported that 3 patients (3.2%) migrated to a surgical approach due to tumor progression. Miyauchi et al.¹⁴ observed that 8% of patients presented with increased tumoral volume and 3.8% developed new lymph node metastases during follow-up. Whereas Moon et al.¹⁷ reported an overall progression rate of 5.19%, also resulting in the transition of expectant conduct to surgery^{13,15-17,19}.

There were cases in which tumoral progression did not meet the objective criteria for IS. However, after discussion between the doctor and the patient, they opted to interrupt AS and follow through with surgery^{13,19}. Some of the relevant motivations for loss to follow-up in AS are psychological issues, such as anxiety and fear of tumoral evolution^{1,11,28}.

One study assessed loss to follow-up during the COVID-19 pandemic and analyzed that, before the event, loss to follow-up was significantly lower ($p=0.003$) in AS (17.8%) compared to IS (20.9%). However, in December 2022, after the pandemic event, the percentage of treatments changed to 25.9% and 14%, respectively¹⁴. Data do not allow us to establish causality but suggests a possible correlation.

During discussions on the motivations for loss to follow-up, distance from the medical center, gender, and method of diagnosis presented significant associations²⁴.

Unlike IS, whose loss to follow-up does not enable categorization of a treatment switch to AS, the opposite was an assessed category¹⁷. Therefore, it must be considered that, while loss to follow-up has been greater in most studies in the surveillance modality, this method allows for transition to surgical interventions and has a longer duration.

Assessing both methods, it was observed that AS presented a significantly higher rate of oncological loss to follow-up ($p=0.046$), that is, patients who did not undergo

surgery were more prone to stop attending consultations and exams concerning their tumors. This loss was more evident right after the diagnosis, stabilizing from the second year onwards in both groups²⁵.

Thus, in comparison, regarding loss to follow-up in the current literature, the AS method resulted in higher significant indices.

The analyzed literature presented methodological and contextual limitations that might compromise the generalization and validity of results. Selection biases, as reported in Kong et al., whose study did not randomize patients, enabled more anxious individuals to choose surgery, which could have interfered with the psychological findings. This pattern is also seen in Miyauchi et al.¹⁵, whose choice between AS and surgery was based on the preference of patients, introducing self-selection and impairing direct comparison between groups. Sawka et al.²¹ reinforced this critique, suggesting that the lack of randomization limits causal inference, especially in specialized institutions, where patients' higher education or greater access to information may influence results.

The inadequate timing of follow-up is another limitation verified in literature. Kong et al.¹³ identified that the 8-month period to assess post-surgery quality of life may not be enough to capture permanent effects, while Oda et al. highlighted that a short follow-up period (7 months) underestimates risks, such as metastases. Rosario et al.¹⁹ and Sawka et al.²⁰ — ongoing cross-sectional studies — lack long-term data, essential to the analysis of outcomes like quality of life, tumor evolution, and follow-up.

Methodological limitations include collection instruments that are liable to bias. Lai et al.²⁴ used a Markov model with low validation, which can cause inconsistencies in cost-effectiveness projections. In Sugitani et al.²², the applied questionnaire was not previously validated or piloted, in addition to having a response bias due to a lack of anonymization. According to Sawka et al.¹¹, the lack of tools to assess post-surgical fear is noteworthy, limiting the precision of findings.

Geographic and cost variability compromises global applicability. Lin et al.²⁷ considered the Australian healthcare system, while Lai et al.²⁴ and Oda et al.¹⁸ highlighted significant differences in procedure prices in countries such as China, Japan, and the USA. Faro et al.²⁹ warned that cost analyses in Brazil considered only SUS prices, not assessing the reality of the private sector.

Reduced sample sizes and lack of diversity are other valid points for analysis. Two studies worked with small samples from a single institution, limiting

representativeness^{1,3}. D'Agostino et al.²⁸ and Smulever et al.³⁰ highlight that homogeneous samples (high education in Sawka et al.²¹) or loss to follow-up (as in Miyauchi et al.¹⁴, due to the COVID-19 pandemic) distort results.

Cultural and emotional factors also influence the findings. Smulever et al.³⁰ observed that the preference for more aggressive surgeries, even when unnecessary, is connected to anxiety and poor access to healthcare. Rosario et al.¹⁹ highlighted that AS acceptance varies culturally, being more adopted in contexts in which cancer diagnosis causes greater stigma.

Finally, reference biases and institutional contexts are also highlighted. Sawka et al.¹¹ noticed that patients referred by external specialists may have distinct clinical profiles, while Molinaro et al.¹⁶ and Nakamura et al.²³ were limited to data from unique centers in Italy and Japan, respectively.

The studies analyzed present gaps that require caution in interpretation. The combination of selection biases, short follow-up, restricted samples, and contextual variability requires further multicentric, randomized studies with validated instruments, in addition to cost analyses adapted to each healthcare system.

The present study presents some limitations, since this review used only the PubMed and Embase databases, which could have resulted in the exclusion of possibly relevant studies for this review.

Another point to consider is the sample size, which resulted in only 24 articles read in full that had enough scientific foundation to meet the inclusion criteria of a bibliographical review, which might have contributed to the limitation on the amount of data for review.

Additionally, some articles could have been misinterpreted upon full reading. This limitation was minimized by dividing the article reading between two team members, which contributed to a more balanced and enhanced analysis of the selected studies.

As valuable as the results presented are, methodological limitations, such as lack of randomization and geographic variability, impair direct comparison between these two approaches. It is also noteworthy that the profile of patients differed between the studies, in addition to addressing issues, medical practices, and characteristics specific to each article's country of origin, for instance, the cost of thyroidectomy.

In general, the methodological assessment evidenced heterogeneity in the quality of the included studies. Among the cohorts, confounding bias constituted the main methodological limitation, while the studies assessed by Drummond's and JBI's instruments presented mostly satisfactory methodological quality, with a few limitations related to the control of confounding factors, measurement

of outcomes, and specific aspects of economic assessments. These findings should be considered when interpreting the results of this review.

The lack of consensus among studies that assessed quality of life probably comes from the methodological heterogeneity observed in the included studies. Differences related to the instruments used for assessing the outcomes, duration of follow-up, clinical profile of patients, and criteria for referring to AS impaired direct comparisons between the studies. Furthermore, quality of life represents a multifactorial outcome, influenced not only by the physical repercussions of the treatment but also by emotional, cultural, and individual factors. Therefore, while patients who underwent surgery may present a higher impact from postoperative complications and the need for hormonal therapy, individuals followed up in AS may experience varied levels of anxiety related to living with a cancer diagnosis. This duality probably explains the inconsistency observed among the studies and reinforces the need to use standardized, validated instruments to assess this outcome.

Another noteworthy aspect is the potential selection bias present in most available evidence. Since practically all studies included presented an observational design, the choice between AS and IS was often determined by the patient's and doctor's preference, and not by randomization. Consequently, younger, more anxious individuals, or those concerned about their oncological diagnosis, tend to choose surgery, while elderly patients, with smaller tumors or higher acceptance of the expectant conduct, were frequently directed to AS. Thus, part of the differences observed between groups may reflect distinct characteristics of the studied population and not necessarily the effect of the adopted therapeutic strategy. This aspect makes the interpretation of results particularly relevant in light of the confounding risk identified by the studies' methodological assessment⁹.

Although results from this review generally favor the use of AS in carefully selected patients, the robustness of the evidence must be interpreted with caution. Risk of bias assessment demonstrated that cohort studies presented, as their main methodological limitation, confounding inherent to the lack of randomization and selection of patients according to clinical characteristics and individual preferences. This scenario limits causal inference and reduces direct comparability between therapeutic strategies⁹.

Therefore, although the consistency of results in different studies increases the reliability of conclusions, the need for multicentric prospective studies with improved methodological standardization and proper control of confounding factors remains.



CONCLUSION

In conclusion, this study revealed that AS, in most cases, is a more economical and effective option in terms of survival when compared to IS for patients with thyroid microcarcinoma. However, factors such as age, tumor stage, and location of treatment may influence both the costs and clinical results. Although both groups present limited tumoral growth, AS is associated with a higher rate of loss to follow-up, which may be explained by psychological and logistical factors. The analyses of quality of life between both groups did not provide definitive conclusions, which reinforces the need for further studies in this regard. As valuable as the results presented are, methodological limitations, such as lack of randomization and geographic variability, impair direct comparison between these two approaches.

Thus, so that further studies may provide more consistent evidence, it is necessary to include more diversified samples and more rigorous control of the confounding factors involved. By doing so, it will be possible to improve clinical decision-making and promote better outcomes in the treatment of PTMC.

CONTRIBUTIONS

Mariana Filipak Machado and Lara Terumi Takayama have substantially contributed to the study design and planning; data acquisition, analysis, and interpretation; and wording. Laura Vivacqua de Barros, Lucas Kaiser Gomes da Silva, Guilherme Alves Mariath Costa, and Theo Kaminski de Souza contributed to wording and critical review. All the authors approved the final version for publication.

DECLARATION OF CONFLICT OF INTERESTS

There is no conflict of interest to declare.

DATA AVAILABILITY STATEMENT

All the contents associated with the article are included in the manuscript.

FUNDING SOURCES

None.

REFERENCES

- Griffin A, Brito JP, Bahl M, et al. Applying criteria of active surveillance to low-risk papillary thyroid cancer over a decade: how many surgeries and complications can be avoided? *Thyroid*. 2017;27(4):518-23. doi: <https://doi.org/10.1089/thy.2016.0568>
- Jeon MJ, Lee YM, Sung TY, et al. Quality of life in patients with papillary thyroid microcarcinoma managed by active surveillance or lobectomy: a cross-sectional study. *Thyroid*. 2019;29(7):956-62. doi: <https://doi.org/10.1089/thy.2018.0711>
- Yoshida Y, Horiuchi K, Okamoto T. Patients' view on the management of papillary thyroid microcarcinoma: active surveillance or surgery. *Thyroid*. 2020;30(5):681-7. doi: <https://doi.org/10.1089/thy.2019.0420>
- Smulever A, Pitoia F. High rate incidence of post-surgical adverse events in patients with low-risk papillary thyroid cancer who did not accept active surveillance. *Endocrine*. 2020;69(3):587-95. doi: <https://doi.org/10.1007/s12020-020-02310-8>
- Ouzzani M, Hammady H, Fedorowicz Z, et al. Rayyan-a web and mobile app for systematic reviews. *Syst Rev*. 2016;5:210. doi: <https://doi.org/10.1186/s13643-016-0384-4>
- Barker TH, Hasanoff S, Aromataris E, et al. The revised JBI critical appraisal tool for the assessment of risk of bias for analytical cross-sectional studies. *JBI Evid Synth*. 2026;24(3):401-8. doi: <https://doi.org/10.11124/JBIES-24-00523>
- Drummond MF, Sculpher MJ, Claxton K, et al. Methods for the economic evaluation of health care programmes. 4. ed. Oxford: Oxford University Press; 2015.
- Lockwood C, Porritt K, Munn Z, et al. Systematic reviews of qualitative evidence. In: Aromataris E, Lockwood C, Porritt K, et al., editors. *JBI manual for evidence synthesis*. Adelaide: JBI; 2024. doi: <https://doi.org/10.46658/JBIMES-24-02>
- Sterne JAC, Hernán MA, Reeves BC, et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. *BMJ*. 2016;355:i4919. doi: <https://doi.org/10.1136/bmj.i4919>
- Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ*. 2021;372:n71. doi: <https://doi.org/10.1136/bmj.n71>
- Sawka AM, Ghai S, Rotstein L, et al. A quantitative analysis examining patients' choice of active surveillance or surgery for managing low-risk papillary thyroid cancer. *Thyroid*. 2022;32(3):255-62. doi: <https://doi.org/10.1089/thy.2021.0485>
- Oda H, Miyauchi A, Ito Y, et al. Comparison of the costs of active surveillance and immediate surgery in the management of low-risk papillary microcarcinoma of the thyroid. *Endocr J*. 2017;64(1):59-64. doi: <https://doi.org/10.1507/endocrj.EJ16-0381>

13. Kong SH, Ryu J, Kim MJ, et al. Longitudinal assessment of quality of life according to treatment options in low-risk papillary thyroid microcarcinoma patients: active surveillance or immediate surgery (interim analysis of MAeSTro). *Thyroid*. 2019;29(8):1089-96. doi: <https://doi.org/10.1089/thy.2018.0624>
14. Miyauchi A, Ito Y, Fujishima M, et al. Long-term outcomes of active surveillance and immediate surgery for adult patients with low-risk papillary thyroid microcarcinoma: 30-year experience. *Thyroid*. 2023;33(7):817-25. doi: <https://doi.org/10.1089/thy.2023.0076>
15. Miyauchi A. Clinical trials of active surveillance of papillary microcarcinoma of the thyroid. *World J Surg*. 2016;40(3):516-22. doi: <https://doi.org/10.1007/s00268-015-3392-y>
16. Molinaro E, Campopiano MC, Pieruzzi L, et al. Active surveillance in papillary thyroid microcarcinomas is feasible and safe: experience at a single Italian center. *J Clin Endocrinol Metab*. 2020;105(3):e172-80. doi: <https://doi.org/10.1210/clinem/dgz113>
17. Moon JH, Ryu CH, Cho SW, et al. Effect of initial treatment choice on 2-year quality of life in patients with low-risk papillary thyroid microcarcinoma. *J Clin Endocrinol Metab*. 2021;106(3):724-35. doi: <https://doi.org/10.1210/clinem/dgaa889>
18. Oda H, Miyauchi A, Ito Y, et al. Incidences of unfavorable events in the management of low-risk papillary microcarcinoma of the thyroid by active surveillance versus immediate surgery. *Thyroid*. 2016;26(1):150-5. doi: <https://doi.org/10.1089/thy.2015.0313>
19. Rosario PW, Mourão GF, Calsolari MR. Active surveillance in adults with low-risk papillary thyroid microcarcinomas: a prospective study. *Horm Metab Res*. 2019;51(11):703-8. doi: <https://doi.org/10.1055/a-1015-6684>
20. Sawka AM, Ghai S, Yoannidis T, et al. A prospective mixed-methods study of decision-making on surgery or active surveillance for low-risk papillary thyroid cancer. *Thyroid*. 2020;30(7):999-1007. doi: <https://doi.org/10.1089/thy.2019.0592>
21. Sawka AM, Ghai S, Rotstein L, et al. Decision regret following the choice of surgery or active surveillance for small, low-risk papillary thyroid cancer: a prospective cohort study. *Thyroid*. 2024;34(5):626-34. doi: <https://doi.org/10.1089/thy.2023.0634>
22. Sugitani I, Ito Y, Miyauchi A, et al. Active surveillance versus immediate surgery: questionnaire survey on the current treatment strategy for adult patients with low-risk papillary thyroid microcarcinoma in Japan. *Thyroid*. 2019;29(11):1563-71. doi: <https://doi.org/10.1089/thy.2019.0211>
23. Nakamura T, Miyauchi A, Ito Y, et al. Quality of life in patients with low-risk papillary thyroid microcarcinoma: active surveillance versus immediate surgery. *Endocr Pract*. 2020;26(12):1451-7. doi: <https://doi.org/10.4158/EP-2020-0201>
24. Lai M, Zhang MM, Qin QQ, et al. Cost-effectiveness of active surveillance versus early surgery for thyroid micropapillary carcinoma based on diagnostic and treatment norms in China. *Front Endocrinol (Lausanne)*. 2023;14:1166433. doi: <https://doi.org/10.3389/fendo.2023.1166433>
25. Saito Y, Matsuzaki K, Takami H, et al. Active surveillance vs. surgery in low-risk papillary thyroid microcarcinoma patients and the risk of loss to follow-up. *Cancer Med*. 2024;13(16):e70123. doi: <https://doi.org/10.1002/cam4.70123>
26. Sasaki T, Miyauchi A, Fujishima M, et al. Comparison of postoperative unfavorable events in patients with low-risk papillary thyroid carcinoma: immediate surgery versus conversion surgery following active surveillance. *Thyroid*. 2023;33(2):186-91. doi: <https://doi.org/10.1089/thy.2022.0444>
27. Lin JF, Jonker PKC, Cunich M, et al. Surgery alone for papillary thyroid microcarcinoma is less costly and more effective than long term active surveillance. *Surgery*. 2020;167(1):110-6. doi: <https://doi.org/10.1016/j.surg.2019.05.078>
28. D'Agostino TA, Shuk E, Maloney EK, et al. Treatment decision making in early-stage papillary thyroid cancer. *Psychooncology*. 2018;27(1):61-8. doi: <https://doi.org/10.1002/pon.4383>
29. Faro FN, Bertelli AAT, Scalissi NM, et al. Active surveillance versus immediate surgery in the management of low-risk papillary thyroid microcarcinoma: comparison of long-term costs in Brazil. *Arch Endocrinol Metab*. 2024;68:e230349. doi: <https://doi.org/10.20945/2359-4292-2023-0349>
30. Smulever A, Pitoia F. Active surveillance in papillary thyroid carcinoma: not easily accepted but possible in Latin America. *Arch Endocrinol Metab*. 2019;63(5):462-9. doi: <https://doi.org/10.20945/2359-3997000000168>

Recebido em 13/1/2026
Aprovado em 7/7/2026

