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Research

Global research landscape on active surveillance for papillary thyroid microcarcinoma: a bibliometric analysis

Dong-Shu Kang¹ · Yu-Hao Lin¹ · Jian-Qing Tian¹

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Abstract

Background It has been proven that the active surveillance (AS) is safe and feasible for low-risk papillary thyroid micro-carcinomas (PTMC). There has been no bibliometric assessment of the scientific advancements in this field. We conducted this study to determine the characteristics and trends of published research on AS for PTMC.

Methods In this study, articles on AS for PTMC published between 2014 and 2024 were identified using the Web of Science Core Collection database. Bibliometric analysis and visualization were conducted using VOSviewer and CiteSpace. Results 277 publications from 39 countries were identified, demonstrating a growth trend between 2014 and 2024. The United States of America dominated with the highest number of published papers, followed closely by South Korea and Japan. The most significant journal was *Thyroid*, and the leading author was Akira Miyauchi. Kuma Hospital and Memorial Sloan Kettering Cancer Center emerged as leading institutions. Keyword analysis revealed that, alongside the title-related terms of this study, "management," "quality of life," "lymph node metastasis," "progression," and "association quidelines" formed the core keywords in this field.

Conclusion Active surveillance for low-risk PTMC has been endorsed and recommended by researchers in numerous countries. This study identified the current most active frontiers in this field and focused on candidate population profiling, tumor progression evaluation, cost-effectiveness of the active surveillance (AS) approach, and quality of life assessment for patients. This paper summarizes the controversial issues and provides a reference direction for researchers seeking to explore novel approaches in this field.

Keywords Papillary thyroid microcarcinoma · Active surveillance · Bibliometric analysis · Research trends · Hotspots

1 Introduction

The thyroid cancer incidence in the United States has more than tripled over the past four decades, primarily driven by rising papillary thyroid cancer (PTC) cases [1]. Previous research has emphasized surgery as the initial and crucial step in treating thyroid cancer, aiming to remove all malignant lesions to achieve a cure, improve survival rates, and reduce recurrence risk [2, 3]. Emerging evidence indicates the potential for overdiagnosis and overtreatment of asymptomatic low-risk papillary thyroid microcarcinomas (PTMCs) detected incidentally, especially since thyroid cancer mortality rates have remained stable [4, 5]. PTMCs are defined as papillary thyroid carcinomas with a maximum diameter of 1.0 cm or less [6]. They generally lack malignant features like invasive growth or lymph node metastasis, and tend to remain stable for extended periods. Consequently, they have a limited impact on the quality of life and life expectancy. Active surveillance (AS), which may serve as a more prudent alternative for low-risk

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PTMCs, was first introduced in Japan during the 1990s [7, 8]. Studies on PTC patients, initially conducted in Japan and later expanded globally, have shown that AS leads to favorable outcomes with minimal cancer progression and lymph node metastasis [9–12]. These studies have greatly influenced thyroid cancer management guidelines globally. In 2015, the American Thyroid Association (ATA) guidelines recommended AS as an alternative to immediate surgery (IS) for certain specific cases of PTC [13]. Various international guidelines have since provided recommendations to consider AS for PTC.

Although AS has gained a degree of consensus, the path to clinical practice has not been smooth. In fact, AS is not widely prevalent outside of Japan. In 2018, 53.8% of adults with low-risk PTMC in Japan received AS [14]. Around the same time, survey data from the United States indicated that 44% of practitioners utilized AS in their practice [15]. In Brazil, where data was reported in 2020, only 23% of doctors recommended AS [16]. However, the adoption rate of AS is currently probably lowest in China [17]. There are multiple variables involved in the decision to pursue AS for the management of thyroid cancer, which include physician factors, disease parameters, patient factors, cost-effectiveness, and the structure of the health care system [18–20]. To date, active surveillance for PTMC is still of great interest, and an increasing amount of literature is emerging. However, this area has not been systematically studied through bibliometrics and visual analysis.

Bibliometric analysis uses quantitative mathematical and statistical techniques to examine knowledge domains in a specific discipline. This method facilitates the identification of research priorities, field-specific hotspots, and the assessment of scientific productivity at the levels of countries, institutions, and researchers [21]. This study utilized bibliometric methods to examine articles on AS for PTMC published from 2014 to 2024, highlighting the characteristics and current research trends in the field.

2 Methods

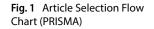
2.1 Data source and literature search strategy

This study was conducted using the Web of Science Core Collection (WoSCC) as a source of literature. The search format is presented as follows: TS = Thyroid carcinoma OR TS = Thyroid cancer OR TS = papillary thyroid microcarcinoma OR TS = thyroid microcarcinoma OR TS = thyroid papillary cancer AND TS = active surveillance. The time period for the article was set from January 1, 2014, to September 10, 2024. The language type was set to English. The publication type was set to 'articles and reviews.' A total of 588 articles were retrieved. The search results and screening process are presented in accordance with PRISMA Flowchart to ensure the transparency and reproducibility of the study, as shown in Fig. 1. Documents retrieved from the Web of Science were exported in plain text format and included both complete records and cited references.

2.2 Statistical methods

Microsoft Office Excel 2019 (Microsoft, Redmond, WA, USA) was employed for the publication trend statistics, data collation, and related tables. VOSviewer (version 1.6.20) and CiteSpace (version 6.3.R2; 64-bit) were used for the bibliometric analysis and visualization. CiteSpace was a software that focused on exploring the potential knowledge contained in scientific literature. It enabled researchers to understand better and grasp the context, mainstream themes, evolving trends, and cutting-edge content of the discipline through data visualization and analysis methods. VOSviewer is an analysis software used to build visual bibliometric graphs. Its main functions include visualization effect display, bibliometrics, cooperative networks, keyword co-occurrence, and topic evolution analysis. In this study, CiteSpace (version 6.3.R2; 64-bit) was used to analyze the publications count of countries, institutions, journals and authors, keywords centrality and frequency, keywords and references outbreaks. VOSviewer (version 1.6.20) explored collaborative networks among authors, institutions, countries, journals, and co-occurrence analysis of keywords and co-citations.



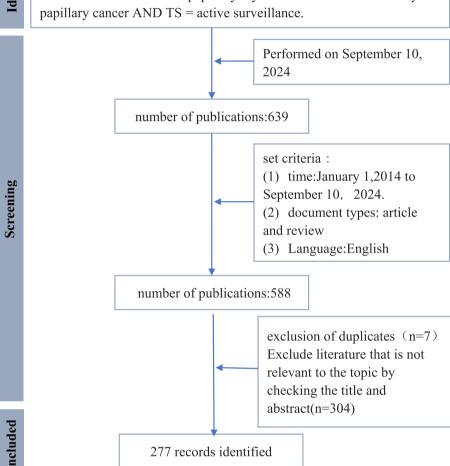


Identification of studies via databases

Identification

Retrieval Database: Web of Science Core Collection(WOSCC)

Search Strategy: TS = Thyroid carcinoma OR TS = Thyroid cancer OR TS = papillary thyroid microcarcinoma OR TS = thyroid microcarcinoma OR TS = papillary thyroid carcinoma OR TS = thyroid papillary cancer AND TS = active surveillance.



3 Results

3.1 Posting trends

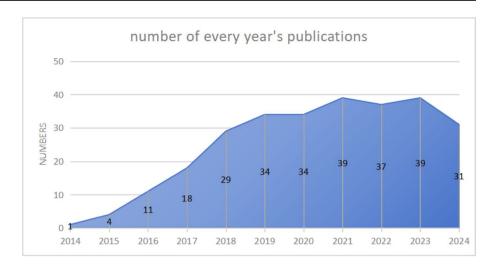
From 2014 to 2024, 277 papers were identified in this research domain through comprehensive manual screening. Figure 2 presents the yearly distribution of these publications. Notably, the publication count exhibited a steady increase from 2015, reaching a peak in 2021 with 39 papers, followed by stabilization between 2022 and 2023.

3.2 Analysis of national or regional cooperation networks

A total of 39 different countries and regions have provided publications in this field. The scientific output of these countries is presented in Fig. 3c and Table 1. The results reveal that the United States holds a leading position in this domain, with a total of 78 publications (28.16%), followed by South Korea (n = 48, 17.33%) and Japan (n = 44, 15.88%). This ranking demonstrates that these three countries play a significant role in AS research for PTMC. Notably, Japan has the highest



Fig. 2 The number of publications per year from 2014 to 2024



citations per publication, signifying its substantial academic impact and indicating that Japanese research outputs have garnered considerable attention and recognition within the scholarly community.

Figure 3a illustrates a cooperation network among countries/regions. Total link strength (TLS) represents both activity and influence within the field of research. The United States demonstrates the strongest international cooperation network (TLS = 41). Figure 3b further reveals that countries such as China, Brazil, and Colombia have recently strengthened their research collaborations.

3.3 Analysis of the contributions by institutions

The study involved 410 institutions, and the top 10 accounted for 40.98% of the total output. Table 2 demonstrates the top 10 prolific institutions, the majority of which are from the United States, South Korea, and Japan. Kuma Hospital made the highest contribution, with 36 papers and 2095 citations, followed by Memorial Sloan Kettering Cancer Center (26 papers, 1424 citations) and the University of Ulsan (18 papers, 707 citations). An institutional cooperation analysis revealed the collaborations between institutions (Fig. 4a). Memorial Sloan Kettering Cancer Center exhibits the largest cooperative network (TLS=81). Furthermore, Fig. 4b demonstrates the significance of institutions as intermediaries, with Memorial Sloan Kettering Cancer Center, Columbia University, and Kuma Hospital displaying high centrality scores ($^{>}$ 0.1).

3.4 Journals and co-cited journals

One hundred one journals published research or review articles in this area. Table 3 lists the top 10 journals by productivity, including their total citations and total number of publications. Notably, most of the top 10 journals were classified as JCR Q1 and Q2, indicating high quality. *Thyroid* led with the highest publication count of 51, followed by *Frontiers in Endocrinology* (16 papers) and *Clinical Endocrinology & Metabolism* (9 papers). A collaborative network of journals is illustrated in Fig. 5a, where each circle represents a journal, and the size of each circle indicates the publication output. In addition, Fig. 5b illustrates the visualization of a co-citation network for journals that have received at least 25 citations. The journal *Thyroid* had the highest total citations, with 2,333 (IF = 5.8), followed by *Journal of Clinical Endocrinology & Metabolism* with 530 (IF = 5.0) and *Surgery* with 374 (IF = 3.2). The notably greater number of citations and publications for *Thyroid* in comparison to other journals highlights its significant impact and productivity.

3.5 Analysis of contributions of prolific authors and co-cited authors

Between 2014 and 2024, 1179 researchers and 3250 co-cited authors contributed to the field. Tables 4 and 5 reveal that the top 10 most prolific and co-cited authors were from South Korea, Japan, and the United States. The top 10 most prolific authors collectively published 162 articles (58.48%) in the field. Akira Miyauchi led with the highest number of publications (34, 12.27%), followed by Ito Yasuhiro (30, 10.83%) and Juan P. Brito (14, 5.05%). Table 5 illustrates that Ito Yasuhiro (819), I. Sugitani (325), and Akira Miyauchi (296) topped the co-cited author list with the highest number of citations. These results suggest that the authors mentioned earlier have demonstrated a higher level of interest in this area.



Fig. 3 a Network visualization map of the countries' collaboration. b Overlay visualization map of the countries' collaboration. c Bar graph of the top ten productive countries/ regions

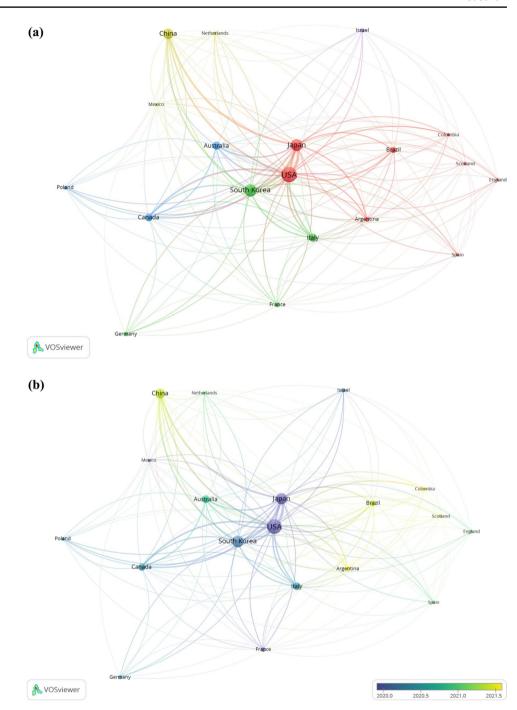


Figure 6a illustrates a cooperative network of authors with over 5 publications, containing 5 clusters, 63 nodes, and 357 connections. Notably, Akira Miyauchi was the author with the highest total link strength (TLS = 143). Figure 6b shows a co-cited author analysis diagram.

3.6 Analysis of highly cited references

The 10 highly cited articles have been cited 1,971 times (39.71%), with each receiving more than 100 co-citations. Among these top 10 publications, five were from Japan, three from the United States, and the remaining two from South Korea and France (Table 6). The most cited article among the top 10, "Natural History and Tumor Volume Kinetics of Papillary Thyroid Cancers During Active Surveillance," was published in JAMA Otolaryngology-Head & Neck Surgery in 2017.



Fig. 3 (continued)

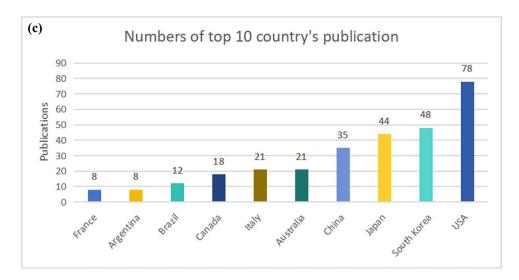


Table 1 The top 10 most productive countries/regions

Rank	Countries/region	Publication	Proportion of publication	Citations	Citations per publication
1	USA	78	28.16%	2594	33.26
2	South Korea	48	17.33%	1203	25.06
3	Japan	44	15.88%	2414	54.86
4	China	35	12.64%	247	7.06
5	Australia	21	7.58%	432	20.57
6	Italy	21	7.58%	617	29.38
7	Canada	18	6.50%	405	22.50
8	Brazil	12	4.33%	94	7.83
9	Argentina	8	2.89%	77	9.63
10	France	8	2.89%	304	38.00

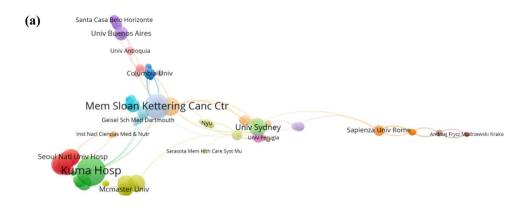
Table 2 The top 10 most productive institutions

Rank	Institutions	Publication	Citations	Country	Citations per publication
1	Kuma Hospital	36	2095	Japan	58.19
2	Memorial Sloan Kettering Cancer Center	26	1424	USA	54.77
3	University of Ulsan	18	707	South Korea	39.28
4	Mayo clinic	14	487	USA	34.79
5	Seoul National University	13	233	South Korea	17.92
6	The University of Sydney	13	303	Canada	23.31
7	University of Toronto	13	218	USA	16.77
8	National Cancer Center	12	186	Japan	15.50
9	University Health Network	12	228	Australia	19.00
10	Sungkyunkwan University	11	495	South Korea	45.00

Figure 7a displays a network graph of highly co-cited references, organized into three distinct clusters, each represented by a different color: green, blue, and red. A burst analysis of co-cited references was conducted using CiteSpace. Citation bursts identified references that were widely cited over time, highlighting their findings as well-established in this field. These bursts signify that a reference has been frequently cited over time, indicating that the study's findings are well-recognized in the field (Fig. 7b). The green line indicates the period between 2014 and



Fig. 4 a Analysis of the contributions by institutions. **b** Intermediary centrality of institutions



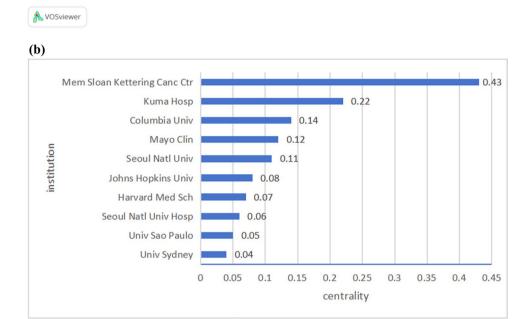


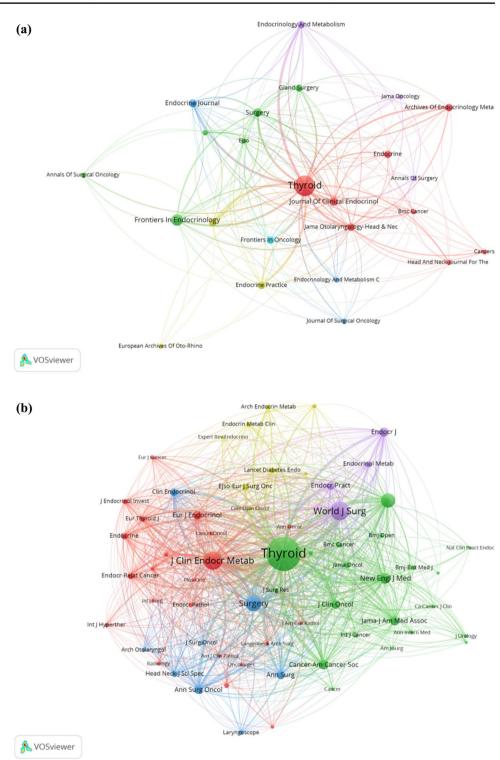
Table 3 The core journals that published publications in the field of active surveillance for PTMC

Rank	Journal	NP	TC	IF2024	JCR quartile	Categories
1	THYROID	51	2333	5.8	Q1	Endocrinology & metabolism
2	Frontiers In Endocrinology	16	107	3.9	Q2	Endocrinology & metabolism
3	Journal Of Clinical Endocrinology & Metabolism	9	530	5.0	Q1	Endocrinology & metabolism
4	Surgery	9	374	3.2	Q1	Surgery
5	Endocrine Journal	8	201	1.3	Q4	Endocrinology & metabolism
6	Archives Of Endocrinology Metabolism	7	57	1.6	Q4	Endocrinology & metabolism
7	Endocrine	7	35	3.0	Q2	Endocrinology & metabolism
8	Endocrine Practice	7	133	3.7	Q2	Endocrinology & metabolism
9	Endocrinology And Metabolism	7	130	3.9	Q2	Endocrinology & metabolism
10	Frontiers In Oncology	7	50	3.5	Q2	Oncology

 $NP, Number\ of\ published; TC, Total\ citations$



Fig. 5 a The bibliographic coupling network of journals related to PTMC active surveillance. Each circle in the figure represents a journal, and the size of the circle indicates the number of publications output in that journal. **b** The cocitation network visualization of journals with a minimum of 25 citations. The size of the circle indicates the number of citations in that journal



2024, while the periods of each burst keyword are plotted with a red line. The reference with the strongest citation bursts was 'Patient age is significantly related to the progression of papillary microcarcinoma of the thyroid under observation' (Strength: 28.11; Publication Year: 2014), followed by 'Current thyroid cancer trends in the United States' (Strength: 16.04; Publication Year: 2014) and 'Indications and Strategy for Active Surveillance of Adult Low-Risk Papillary Thyroid Microcarcinoma: Consensus Statements from the Japan Association of Endocrine Surgery Task Force on Management for Papillary Thyroid Microcarcinoma' (Strength: 15.42; Publication Year: 2021).



Table 4 The publication count and H-index for the top 10 productive authors

Rank	Author	Country	Documents	Citation	Citations per publication	H-index
1	Miyauchi, Akira	Japan	34	1941	57.09	59
2	Ito, Yasuhiro	Japan	30	1676	55.87	52
3	Brito, Juan P	USA	14	695	49.64	46
4	Kudo, Takumi	Japan	13	471	36.23	29
5	Jeon, Min Ji	South Korea	12	423	35.25	29
6	Kim, Won Bae	South Korea	12	533	44.42	59
7	Kim, Won Gu	South Korea	12	534	44.50	40
8	Shong, Young Kee	South Korea	12	637	53.08	46
9	Tuttle, R. Michael	USA	12	1108	92.33	64
10	Goldstein, David P	Canada	11	171	15.55	46

Table 5 Top 10 co-cited authors

Rank	Co-cited author	Country	Total citation
1	Ito, Y	Japan	819
2	Sugitani, I	Japan	325
3	Miyauchi, A	Japan	296
4	Davies, L	USA	257
5	Haugen, Br	USA	247
6	Tuttle, Rm	USA	244
7	Oda, H	Japan	159
8	Brito, JP	USA	151
9	Jeon, MJ	South Korea	127
10	Oh, HS	South Korea	127

3.7 Analysis of keywords

3.7.1 Keyword co-occurrence

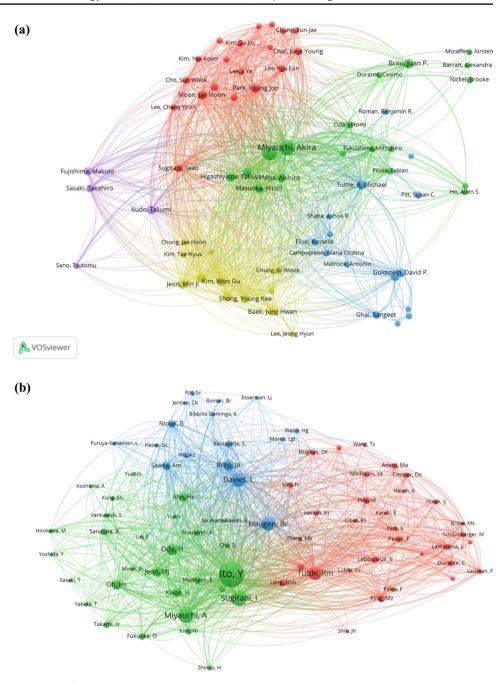
High-frequency keywords indicate the emphases and hotspots in research. Figure 8a displays a network graph of keyword co-occurrence analysis. The node size in the figure represents the frequency of the keywords. The intermediary centrality of keywords was calculated using CiteSpace software, which revealed the following core keywords, except for those related to the title of this paper: 'management,' quality of life,' lymph node metastasis,' progression,' and 'association guidelines' (Table 7).

3.7.2 Keyword bursts analysis

In spite of the effectiveness of VoSviewer in displaying co-occurrences, it does have limitations in showing changes in keyword prominence. Keyword burst analysis, which was generated by CiteSpace software, can be used to visualize the dynamics of discipline development, specifically focusing on the top 15 keywords. As indicated in Fig. 8b, in the past five years, the keywords observed with citation bursts were "low risk (strength 2.81)," "cost effectiveness (strength 2.55)," "watchful waiting (strength 3.1)," "retrospective analysis (strength 1.96)," "prognostic significance (strength 2.14)," "lobectomy (strength 2.33)," and "papillary thyroid carcinoma (strength 1.94)."



Fig. 6 a A collaborative network of authors with more than five publications. The size of the nodes represents the number of articles. b Analysis map of co-cited authors with a minimum of 20 citations. The size of the nodes represents the number of Total citation



4 Discussion

4.1 Basic information

Bibliometric methods were employed to analyze the progression of AS research for PTMC from 2014 to 2024. The literature utilized in the study was retrieved from the WoSCC database. This scientometric study included 277 English papers from 410 different journals, featuring 4,963 co-cited references, and involved 101 institutions across 39 countries/regions after excluding studies that failed to meet the screening criteria. The study outcomes indicate that this topic has recently received significant attention, as evidenced by the steady upward trend in publication count.

VOSviewer

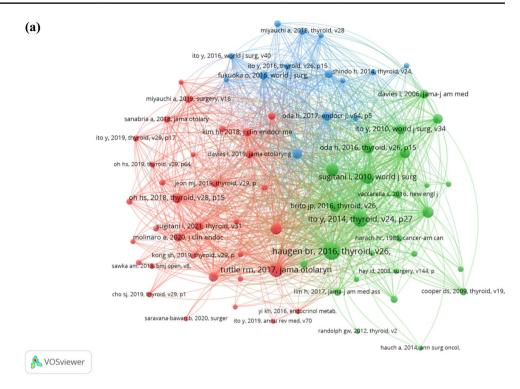


Table 6 The characteristics of highly cited and the most impact classic articles in the field of active surveillance for PTMC

Rank	Rank Total citations Article title	Article title	Journal	Published year Country	Country	IF2024
_	310	Natural History and Tumor Volume Kinetics of Papillary Thyroid Cancers During Active Surveillance	Jama Otolaryngology-head & Neck Surgery	2017	USA	4.0
7	241	Incidences of Unfavorable Events in the Management of Low-Risk Papillary Microcarcinoma of the Thyroid by Active Surveillance Versus Immediate Surgery	THYROID	2016	Japan	5.8
m	221	A Clinical Framework to Facilitate Risk Stratification When Considering an Active Surveillance Alternative to Immediate Biopsy and Surgery in Papillary Microcarcinoma	THYROID	2016	USA	5.8
4	209	Low-risk papillary microcarcinoma of the thyroid: A review of active surveillance trials	European Journal of Surgical Oncology	2018	Japan	3.5
5	199	Indications and Strategy for Active Surveillance of Adult Low-Risk Papillary Thyroid Microcarcinoma: Consensus Statements from the Japan Association of Endocrine Surgery Task Force on Management for Papillary Thyroid Microcarcinoma	THYROID	2021	Japan	5.8
9	178	Papillary thyroid microcarcinoma: time to shift from surgery to active surveillance?	Lancet Diabetes & Endocrinology	2016	France	0.44
^	167	Clinical Trials of Active Surveillance of Papillary Microcarcinoma of the Thyroid	World Journal Of Surgery	2016	Japan	2.3
œ	159	Thyroid surgery for differentiated thyroid cancer—recent advances and future directions	Nature Reviews Endocrinology	2018	USA	36.0
6	151	Active Surveillance for Patients With Papillary Thyroid Microcarcinoma: A Journal of Clinical Endocrinology and Metabolism 2017 Single Center's Experience in Korea	Journal of Clinical Endocrinology and Metabolism	2017	South Korea	5.0
10	136	Insights into the Management of Papillary Microcarcinoma of the Thyroid THYROID	THYROID	2018	Japan	5.8



Fig. 7 a Cluster mapping of highly co-cited literature. b Top 10 references with strongest citation bursts. The green line segment indicates the time interval, while the red line segment indicates the time of frequent citations



(b) Top 10 References with the Strongest Citation Bursts

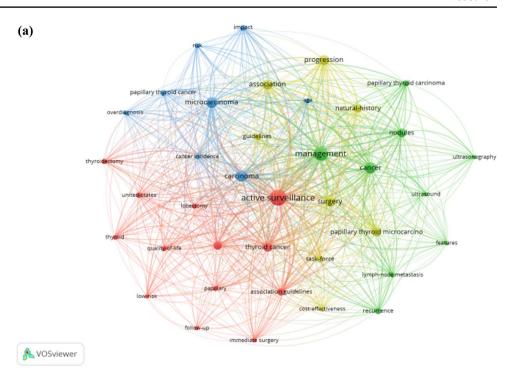
References	Year	Strength	Begin	End	2014 - 2024
Ito Y, 2014, THYROID, V24, P27, DOI 10.1089/thy.2013.0367, DOI	2014	28.11	2015	2019	
Davies L, 2014, JAMA OTOLARYNGOL, V140, P317, DOI 10.1001/jamaoto.2014.1, DOI	2014	16.04	2016	2019	
Ahn HS, 2014, NEW ENGL J MED, V371, P1765, DOI 10.1056/NEJMp1409841, DOI	2014	14.48	2016	2019	
Sugitani I, 2014, WORLD J SURG, V38, P673, DOI 10.1007/s00268-013-2335-8, DOI	2014	7.37	2016	2019	
Shindo H, 2014, THYROID, V24, P840, DOI 10.1089/thy.2013.0527, DOI	2014	6.26	2016	2019	
Haugen BR, 2016, THYROID, V26, P1, DOI 10.1089/thy.2015.0020, DOI	2016	11.89	2017	2019	
Oda H, 2016, THYROID, V26, P150, DOI 10.1089/thy.2015.0313, DOI	2016	7.08	2017	2019	
Nikiforov YE, 2016, JAMA ONCOL, V2, P1023, DOI 10.1001/jamaoncol.2016.0386, DOI	2016	6.32	2017	2019	
Sawka AM, 2020, THYROID, V30, P999, DOI 10.1089/thy.2019.0592, DOI	2020	6.67	2021	2024	
Sugitani I, 2021, THYROID, V31, P183, DOI 10.1089/thv.2020.0330, DOI	2021	15.42	2022	2024	

The key inflection points occurred in 2015 and are potentially linked to the approval for active surveillance of very low-risk PTMC in the 2015 American Thyroid Association guidelines.

The analysis of national publication data reveals that the USA, South Korea, and Japan have emerged as the leading contributors, with the highest number of publications. This indicates that they possess significant influence and leadership in this area. Notably, the United States leads in publication volume and has the strongest international cooperation network, while Japan has the highest citations per publication. The reason for this difference may be that the United States has many of the world's top institutions and hospitals, which have invested heavily in scientific research, and conduct extensive research. In contrast, research in Japan started earlier, and long-term prospective studies have accumulated a wealth of high-quality data. Of course, many factors, such as research collaboration and exchange, academic journals and review systems, sociocultural and medical practices, also play a role. Kuma Hospital made the highest contribution, being the first institution to initiate research on thyroid cancer. Thyroid stands out as a significant journal based on publication numbers and citations. Akira Miyauchi from Kuma Hospital published the most papers (34, 12.27%). Among the 10 most-cited articles, in addition to the consensus statement of the Japanese Society of Endocrine Surgery and the review paper on AS, "the decision framework suggesting risk stratification," "the natural history of tumors," and "tumor volume dynamics" have also garnered attention from researchers.



Fig. 8 a A network graph of Keyword co-occurrence analysis. b Top 15 keywords with the most robust citation bursts. The year represented by the red line indicates the time period when the keyword was mainly influential



(b)

Top 15 Keywords with the Strongest Citation Bursts

Keywords	Year	Strength	Begin	End	2014 - 2024
carcinoma	2015	3.61	2016	2016	_
tumors	2016	2.4	2016	2017	
patient age	2016	2.14	2016	2020	
papillary microcarcinoma	2017	3.27	2017	2017	
encapsulated follicular variant	2017	3.01	2017	2018	
overdiagnosis	2017	2.64	2017	2018	
lymph node metastasis	2016	2.14	2017	2017	
fine needle aspiration	2017	1.95	2017	2018	
low risk	2018	2.81	2020	2020	
cost effectiveness	2017	2.55	2020	2021	
watchful waiting	2021	3.1	2021	2022	
retrospective analysis	2015	1.96	2021	2022	
prognostic significance	2022	2.14	2022	2024	
lobectomy	2018	2.33	2023	2024	
papillary thyroid carcinoma	2019	1.94	2023	2024	



Table 7 The top 20 keywords ranked by frequency and centrality

Rank	Keywords	Frequency	Keywords	Centrality
1	active surveillance	185	Follow up	0.16
2	management	131	Guidelines	0.12
3	carcinoma	90	Papillary thyroid cancer	0.12
4	cancer	89	Carcinoma	0.1
5	progression	67	Association guide	0.1
6	association	66	Lymph node metastasis	0.1
7	microcarcinoma	65	Quality of life	0.1
8	thyroid cancer	59	Thyroid cancer	0.09
9	papillary thyroid microcarcinoma	59	Association	0.08
10	surgery	57	Nodules	0.08
11	nodules	56	Natural history	0.07
12	natural history	52	Task force	0.07
13	papillary microcarcinoma	49	Decision making	0.07
14	association guide	39	Impact	0.06
15	Lymph node metastasis	33	Recurrence	0.06
16	guidelines	30	Cancer incidence	0.06
17	quality of life	30	United States	0.06
18	task force	29	central neck dissection	0.06
19	papillary thyroid carcinoma	28	Active surveillance	0.05
20	papillary thyroid cancer	25	Surgery	0.05

4.2 Research basic knowledge and hot issues

4.2.1 Examine the research foundation based on the co-cited literature.

Co-citations refer to the literature cited in common by researchers. The co-citation analysis aimed to trace the research basics of active surveillance for PTMC. Japanese researchers discovered high rates of latent thyroid cancer in systematic autopsy series of non-thyroid disease victims [22–24]. In 1985, autopsy reports from Finland exhibited a prevalence of 35.6%, the highest reported rate in the world, which was significantly higher than the reported prevalence of clinical thyroid cancer at that time [25]. The scholars hypothesized that most PTMCs remain small and harmless to the hosts, with only a few progressing to clinically significant cancers that could cause damage to the hosts [26]. Serious questions have been raised about whether surgery is necessary for these clinically harmless thyroid microcarcinomas. In 1993, Miyauchi initiated an observational clinical trial for low-risk PTMCs using AS instead of IS. A comparable trial commenced two years later at the Cancer Institute Hospital in Tokyo. Recent epidemiological updates have highlight the growing impact of overdiagnosis and overtreatment [27]. More research has been dedicated to exploring the feasibility of AS.

4.2.2 The research hotspot is explored through keyword co-occurrence and burst analysis

Keywords with high frequency and centrality reveal the hotspots, core, and structural characteristics of a research area. Keyword analysis from this study identified key research hotspots, including "management," "quality of life," "lymph node metastasis," "progression," and "association guidelines." A keyword burst analysis highlights recent trends and hotspots in a scientific field. The recent keyword burst analysis indicated a surge in terms such as "low risk," "cost-effectiveness," "watchful waiting," "prognostic significance," and "lobectomy" over the last five years, providing insights into research trends. We can summarize several key directions for the future of this area.

4.2.2.1 Long-term prognosis This theme included 'lymph node metastasis' and 'prognostic significance,' signifying an ongoing concern for the clinical safety of AS. Akira Miyauchi has updated the report on long-term tumor outcomes



in patients treated with AS for PTMC at 10, 20, and 30 years of follow-up over the past 30 years [8, 12]. It was shown that tumor outcomes were equally good for immediate surgery and active surveillance. Notably, no significant PTC recurrence or death was found in patients who underwent salvage surgery after showing signs of progression, and their postoperative outcomes were not significantly different from those of patients who underwent immediate surgery [8, 28]. Although all these findings appear to support AS for PTMC, it remains an investigational treatment. More data are needed to determine the safety of this treatment method.

4.2.2.2 Evaluation of tumor progression Evaluating tumor progression has always been a significant research challenge and hotspot. Identifying the characteristics of progression can help exclude unsuitable candidates.

A high Ki-67 labeling index, psammoma bodies, and intraglandular metastases indicate progressive PTMC, according to Hirokawa et al. [29]. In 480 lesions from 384 patients, O. Fukuoka et al. found significantly higher rates of calcification and less vascularity in PTMC in older patients [30]. In addition, high thyroid-stimulating hormone (TSH) levels are associated with PTMC progression during AS [31]. An attempt to lower TSH to a low normal range may prevent carcinoma growth [32]. Consequently, tumor proliferative activity, calcification, blood supply, and age are crucial factors for progression in active surveillance. More reliable conclusions can be drawn from prospective studies, however.

4.2.2.3 Patient factor This theme includes 'quality of life,' 'lobectomy,' and 'cost-effectiveness,' serving as a reminder that research in the field has expanded from the assessment of tumor progression and prognosis to a focus on cost-effectiveness and quality of life.

Active Surveillance aims to avoid surgical complications and improve quality of life (QoL), making it one of the critical factors in treatment decisions. A systematic review indicated that QoL scores for the AS group were generally higher than those for the Intervention Surgery (IS) group [33]. However, when it comes to psychological problems, particularly anxiety levels, studies show inconsistent results [34, 35]. Anxiety in patients with IS mainly stems from concerns about the progression of the disease. Such patients may be more inclined to opt for IS to quickly address the disease and reduce the uncertainty associated with long-term monitoring. However, the surgical treatment did not improve their psychological distress or sleep disturbances [36]. Instead, Some AS patients noted that their tumor size did not change during follow-up, which led to a reduction in cancer-related anxiety [37]. Given the complexity of the medical decision-making process, we look forward to reducing patient anxiety about tumors in the future. In addition to providing patients with psychological support and counseling, more evidence on the long-term safety of AS is needed to boost both physician and patient confidence.

Various studies have provided conflicting data on the cost-effectiveness of AS and IS. Lin et al. and Youssef et al. observed that surgery is less costly than AS [38, 39]. However, when quality of life or older age (≥ 69 years) was taken into account, AS appeared to be the preferred choice. A prospective cohort study in South Korea showed no significant difference in cost between the two strategies at 10 years of follow-up, while IS was found to be more cost-effective when a longer follow-up was conducted [40]. Cost-benefit analysis is essentially an analytical method based on assumptions and models. Its accuracy is limited in real clinical situations due to many uncertainties and variables. Various healthcare systems may employ distinct costing methods and criteria. In Japan, the cost of thyroid sonography and physician visit fees is much cheaper than those mentioned in other studies, with active surveil-lance being considered more cost-effective [41]. Furthermore, the lack of established guidelines for determining appropriate AS follow-up endpoints hinders long-term benefit prediction because of the numerous repeated tests and visits. More research is needed to refine the methods and techniques of cost-benefit analysis to improve their accuracy and practicality in actual clinical situations.

4.2.2.4 More comprehensive guidelines This theme includes 'management,' low risk,' and 'association guidelines,' signifying a focus on more refined risk stratification and management strategies.

The concept of AS has been proposed for nearly 30 years, during which the accumulation of multi-country research data has enabled continuous updates to PTMC active monitoring, resulting in the gradual formation of a clinical management framework focused on the characteristics of the tumor, the patient, and the medical team [42]. The growing body of evidence has led to guidelines and associations recommending AS as the initial treatment for selected patients with PTMC [43–46]. However, consensus is lacking regarding the criteria for AS, including tumor size thresholds, follow-up frequency, and the criteria for discontinuing surveillance. More comprehensive guidelines, incorporating the results of recent studies, are also needed to strengthen AS management for PTMC.



4.2.3 Search the latest literature to verify and find new research hotspots

Conducting a systematic review of recent literature is crucial for tracking emerging research issues within the domain and enables researchers to identify current hotspots and trends. To assess the alignment of recent publications with established research trajectories, we analyzed the latest articles on AS for PTMC.

In the past, most published active surveillance data focused on PTCs smaller than 1.0 cm. Studies conducted by the Memorial Sloan Kettering Cancer Center (MSKCC) in the United States examined tumors with a diameter of up to 1.5 cm that were suitable for active surveillance and observed low rates of tumor growth and lymph node metastasis [47]. A recent study further expanded the tumor size range to 1.1–2.0 cm, demonstrating a similar risk of tumor-specific mortality as that of papillary thyroid carcinoma sized 0-1.0 cm [48]. More recently, Benjamin Altshuler et al. examined the feasibility and safety of active surveillance for PTC patients with tumors up to 4 cm in diameter, showing that no new lymph nodes or distant metastases were detected during follow-up of 1 year or more (mean 55 months) [49]. Meanwhile, AS may also be an appropriate strategy for patients with differentiated thyroid cancer (DTC) who have small lymph node involvement, as well as for those with PTC and suspicious cervical lymph node metastasis diagnosed after initial treatment [50, 51]. This suggests that new research is being conducted to expand the criteria for AS candidates.

It remains a priority for researchers to establish a clear definition of disease progression. A retrospective study suggested that an initial tumor volume doubling time (i-TVDT) value of under five years could predict imminent disease progression [52]. Although ultrasound remains crucial for monitoring, challenges associated with assessing progression and minor thyroid abduction highlight the necessity for advanced imaging technologies and multidisciplinary approaches in managing this condition [53].

The question of which molecular markers can effectively predict PTMC disease progression during AS remains debated. In 2018, a review summarized previous studies indicating that the low prevalence of Telomerase Reverse Transcriptase (TERT) promoter mutations in PTMC (4.7%) and the high prevalence of BRAFV600E mutations (64%) may not be reliable biomarkers for identifying stable patients and cases of potential disease progression during AS [54]. In 2020, Cheng et al. demonstrated in a retrospective analysis that the TERT promoter mutation was predictive of lymphovascular invasion in patients with thyroid cancer [55]. However, the latest molecular profiling study indicated that detecting prevalent driver gene mutations, such as BRAF or RAS, does not accurately forecast which PTMC cases will progress during active surveillance [56]. Recently, Chinese researchers analyzed 10 early-stage papillary thyroid carcinomas (PTC) using single-cell RNA sequencing (scRNA-seq) and found that the indolent PTC tumors exhibit higher enrichment of tumor-infiltrating B cells (TIL-B), particularly germinal center B cells (GC-B). Markers such as LMO2, which is associated with GC-B cells, may serve as potential diagnostic and prognostic indicators for indolent PTC [57]. Active surveillance of thyroid cancer is a growing field, with the study of molecular markers as a key direction expected to provide more information and options for the management and treatment of the disease in the future.

4.3 Limitations

This paper has several limitations. The data were sourced exclusively from the WOSCC database, potentially omitting research from some countries. Additionally, the analysis was restricted to English literature, excluding research in other languages, which may introduce bias. Recent high-quality articles may not have received sufficient attention due to their short publication time frame and low citation frequency, requiring a need for updates in future research. Additionally, it cannot be guaranteed that all publications meet the relevant topic search criteria. The focus on AS literature for PTMC from 2014 to 2024 also excludes earlier papers. Despite these limitations, the results presented in this paper are sufficient to indicate the current state of the field.

5 Conclusions

In summary, the volume of research papers about AS of PTMC has demonstrated a consistent upward trend from 2014 to the present. Japan, South Korea, and the United States have been influential in advancing research within this domain. This analysis delineates current focal points in the field while also investigating prospective directions for future investigation. Prominent research topics concerning AS of PTMC include long-term tumor prognosis, disease progression assessment, quality of life considerations, and cost-effectiveness analyses. Future avenues may involve establishing more precise candidate criteria and identifying molecular markers predicting disease progression. These investigative pathways



will significantly influence the formulation of evidence-based guidelines and consensus statements. Overall, this study elucidates historical and contemporary trends in AS research for PTMC, providing valuable insights for researchers and practitioners seeking new exploration opportunities.

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Declarations

Competing interests The authors declare no competing interests.

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