Papillary thyroid microcarcinoma: When less is more

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For decades, a diagnosis of papillary thyroid microcarcinoma (PTMC) often led directly to surgery, despite its indolent nature in many patients. The question of whether active surveillance (AS) could be a safe and effective alternative for low-risk cases has been a persistent clinical dilemma. New long-term data from a Japanese cohort provides compelling evidence that AS is a viable initial management option, sparing many patients from immediate surgical intervention while maintaining excellent oncological outcomes.1

KEY TAKEAWAYS

- The Pivot: Active surveillance for low-risk PTMC demonstrates oncological outcomes comparable to immediate surgery over 10 and 20 years.
- The Data: Immediate surgery resulted in a significantly higher proportion of patients undergoing one or more surgeries (100% vs. 12.3%; p<.01).
- The Action: Clinicians should consider active surveillance as a primary management strategy for adult patients with low-risk PTMC, reserving surgery for documented progression.

Papillary thyroid microcarcinoma, defined as a papillary thyroid carcinoma 10 mm or less in greatest dimension, is increasingly detected due to advances in imaging. While often indolent, the traditional management approach has been immediate surgical resection, carrying inherent risks of complications such as hypoparathyroidism, recurrent laryngeal nerve injury, and the need for lifelong thyroid hormone replacement. The Kuma Hospital in Japan initiated active surveillance for low-risk PTMC patients 30 years ago, providing an invaluable long-term dataset to compare AS with immediate surgery (IS). This retrospective review of extended follow-up data from a single-center, prospective observational study offers a comprehensive look at the oncological outcomes over two decades.1,2,3

The study enrolled 5646 adult patients diagnosed with low-risk PTMC between 1993 and 2019. Low-risk criteria typically include tumors confined to the thyroid, no evidence of lymph node or distant metastases, and no aggressive histological features. Of these, 3222 patients opted for active surveillance, while 2424 underwent immediate surgery. Patients in both groups received regular follow-up, at least annually, allowing for meticulous tracking of tumor progression, new metastases, and surgical interventions. The sheer volume of patients and the extended follow-up period, reaching up to 30 years for some, lend considerable weight to these findings.1,2,3

Comparing Surveillance and Surgical Outcomes

The primary objective of the study was to compare the long-term oncological outcomes between the active surveillance and immediate surgery groups. Researchers meticulously tracked tumor enlargement, novel lymph node metastases, and distant metastatic recurrence. In the active surveillance group, 124 patients (3.8%) experienced tumor enlargement of ≥3 mm. The 10-year enlargement rate was 4.7%, increasing to 6.6% at 20 years. This slow progression rate highlights the

indolent nature of these microcarcinomas in the vast majority of patients.1,2,3

Novel lymph node metastases occurred in 27 patients (0.8%) in the active surveillance group. The 10-year nodal metastasis occurrence rate was 1.0%, rising to 1.6% at 20 years. These rates are remarkably low, suggesting that for most patients, the risk of regional spread during active surveillance is minimal. For those in the immediate surgery group, 13 patients (0.5%) experienced lymph node recurrence postoperatively. The 10-year nodal recurrence rate was 0.4%, increasing to 0.7% at 20 years. While statistically significant (p=.009) for lymph node metastasis rates between the groups (1.1% vs. 0.4% at 10 years and 1.7% vs. 0.7% at 20 years), the absolute differences were small, suggesting limited clinical impact.1,2,3

Eighteen patients (1.4%) who underwent hemithyroidectomy in the immediate surgery group experienced recurrence in the residual thyroid. This highlights that even with surgical intervention, the risk of recurrence is not entirely eliminated. Distant metastatic recurrence was exceedingly rare, observed in only one patient after active surveillance and conversion surgery, and another after immediate surgery. Both patients remained alive 18.4 and 18.8 years after diagnosis, respectively. None of the patients in this extensive study died of thyroid carcinoma, reinforcing the excellent prognosis associated with low-risk PTMC regardless of initial management strategy. The stake here is patient survival.1,2,3

The Burden of Intervention

The most striking difference between the two groups emerged when comparing the burden of surgical intervention. The proportion of patients who underwent one or more surgeries was significantly higher in the immediate surgery group (100% vs. 12.3%; p<.01). Similarly, the rate of patients requiring two or more surgeries was also significantly higher in the IS group (1.07% vs. 0.09%; p<.01). This stark contrast highlights the primary benefit of active surveillance: avoiding unnecessary surgery and its associated risks and costs for the vast majority of patients. For clinicians managing endocrine conditions, understanding the long-term implications of such interventions is paramount, as detailed in resources like the Oxford Handbook of Endocrinology and Diabetes.1,2,3

The decision to convert from active surveillance to surgery was typically driven by tumor enlargement or the development of new lymph node metastases. This approach ensures that only patients with documented progression, who might genuinely benefit from intervention, undergo surgery. The study's findings support active surveillance as an excellent management technique for identifying patients with progressive low-risk papillary thyroid microcarcinoma requiring surgical treatment.3

Levothyroxine Treatment and Outcomes

A related analysis from the same Kuma Hospital cohort explored the impact of levothyroxine treatment status on active surveillance outcomes. While the primary study focused on comparing AS and IS, the role of thyroid-stimulating hormone (TSH) suppression in PTMC management has been a topic of ongoing discussion. This sub-analysis aimed to determine if levothyroxine treatment, often used to suppress TSH levels, influenced tumor progression or metastasis rates in patients undergoing active surveillance.2

The researchers stratified the active surveillance group by levothyroxine treatment status. They found that the long-term oncological outcomes, including tumor enlargement and novel lymph node metastases, generally did not differ clinically significantly based on whether patients were receiving levothyroxine. This suggests that for low-risk PTMC patients on active surveillance, routine TSH suppression with levothyroxine may not offer additional oncological benefit in

preventing progression. This finding could influence future guideline recommendations regarding the necessity of TSH suppression in this specific patient population, potentially reducing polypharmacy and treatment burden. Our previous coverage on hypothyroidism and symptom burden highlights the importance of re-evaluating treatment strategies.

The Clinical Implications of Long-Term Data

These 10- and 20-year outcomes provide robust, real-world evidence supporting active surveillance as a safe and effective initial management strategy for low-risk PTMC. The data challenges the historical default to immediate surgery, demonstrating that for most patients, watchful waiting does not compromise oncological safety. The low rates of tumor enlargement and nodal metastasis, coupled with the absence of thyroid carcinoma-related deaths in either group, offer significant reassurance to both clinicians and patients considering active surveillance.1,2,3

The open-label, retrospective nature of this single-center study is an obvious caveat. While the Kuma Hospital has extensive experience and a well-established protocol for active surveillance, the generalizability of these findings to other healthcare systems with different patient populations, surveillance protocols, or surgical expertise might be debated. But the sheer size of the cohort and the extended follow-up period mitigate some of these concerns, providing a strong foundation for these conclusions. The study was not a randomized controlled trial, which is often considered the gold standard, but the ethical implications of randomizing patients to immediate surgery versus active surveillance for a condition with such an excellent prognosis are complex. The choice between AS and IS was based on patient preference and clinician recommendation, which introduces potential selection bias, though the authors attempted to account for this through careful patient selection for low-risk criteria.1,2,3

Another consideration is the definition of 'low-risk.' While the study used established criteria, variations in imaging techniques and interpretation across different centers could influence patient selection for active surveillance. The expertise of the ultrasonographers and endocrinologists at Kuma Hospital in identifying and monitoring these lesions is likely a significant factor in their successful outcomes. The study also did not examine deeply into the psychological burden of active surveillance, which can be a concern for some patients living with a cancer diagnosis, even if it is indolent. This aspect, while not directly oncological, is an important component of patient-centered care. For more on the prognostic factors in endocrine disease, our insights on biochemical response at 12 months offer additional context. Still, the data unequivocally demonstrates that immediate surgery carries a significantly higher burden of intervention without a corresponding improvement in long-term oncological survival. This evidence should empower clinicians to confidently offer active surveillance as a primary option, reducing overtreatment and improving quality of life for many patients. Future research might focus on identifying even more precise biomarkers to predict which low-risk PTMCs are truly destined for progression, further refining patient selection for active surveillance. The role of molecular testing, as discussed in our piece on Afirma Molecular Testing, could also become more prominent in this context.1,2,3

> **CLINICAL IMPLICATIONS**
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> These long-term outcomes from Kuma Hospital solidify active surveillance as the preferred initial strategy for low-risk papillary thyroid microcarcinoma. For too long, the default has been surgical intervention, often driven by a 'better safe than sorry' mentality that ignores the real risks and burdens of surgery itself. This study provides the definitive data to shift that paradigm.
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> Clinicians should now feel confident in discussing active surveillance as the primary management option with

> eligible patients. The data is clear: the vast majority will not experience clinically significant progression, and those who do can undergo conversion surgery with excellent outcomes. This approach spares patients from unnecessary surgical complications, lifelong hormone replacement, and the associated healthcare costs.
> The finding that levothyroxine treatment did not significantly alter outcomes in the active surveillance group is also noteworthy. It suggests that routine TSH suppression may not be necessary for these low-risk patients, potentially reducing medication burden and side effects. This warrants a re-evaluation of current guidelines that might still recommend TSH suppression in all PTMC cases.
> This study also highlights the importance of patient education and shared decision-making. While the oncological outcomes are reassuring, some patients may still experience anxiety with a 'watch and wait' approach. Providing clear, evidence-based information about the indolent nature of these tumors and the high success rates of active surveillance is important for empowering patients to make informed choices that align with their values and preferences.

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