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ACTIVE SURVEILLANCE FOR PAPILLARY THYROID MICROCARCINOMA: NEW CHALLENGES AND OPPORTUNITIES FOR THE HEALTH CARE SYSTEM

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DISCLOSURE

The authors have no multiplicity of interest to disclose.

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Abstract

Objective—The dramatic increase in papillary thyroid carcinoma (PTC) is primarily a result of early diagnosis of small cancers. Active surveillance is a promising management strategy for papillary thyroid microcarcinomas (PTMCs). However, as this management strategy gains traction in the U.S., it is imperative that patients and clinicians be properly educated, patients be followed for life, and appropriate tools be identified to implement the strategy.

Methods—We review previous active surveillance studies and the parameters used to identify patients who are good candidates for active surveillance. We also review some of the challenges to implementing active surveillance protocols in the U.S. and discuss how these might be addressed.

Results—Trials of active surveillance support nonsurgical management as a viable and safe management strategy. However, numerous challenges exist, including the need for adherence to protocols, education of patients and physicians, and awareness of the impact of this strategy on patient psychology and quality of life. The Thyroid Cancer Care Collaborative (TCCC) is a portable record keeping system that can manage a mobile patient population undergoing active surveillance.

Conclusion—With proper patient selection, organization, and patient support, active surveillance has the potential to be a long-term management strategy for select patients with PTMC. In order to address the challenges and opportunities for this approach to be successfully implemented in the U.S., it will be necessary to consider psychological and quality of life, cultural differences, and the patient's clinical status.

INTRODUCTION

Papillary thyroid carcinoma (PTC) is the most common endocrine malignancy and is readily treated and highly curable in most instances. Recent epidemiologic data from the Surveillance, Epidemiology and End Results (SEER) program reveals a nearly threefold increase in the incidence of thyroid carcinoma between 1975 and 2009 in the U.S. (1). This phenomenon is not isolated to the U.S. (2–4). In South Korea, the reported incidence of thyroid cancer in 2011 was 15 times greater than in 1993 (5). This marked change is primarily attributable to the increased diagnosis of papillary thyroid microcarcinoma (PTMC), or PTC tumors smaller than 1 cm (1,6). In 1975, PTMC comprised 25% of all diagnosed thyroid cancers in the U.S.; by 2009, that proportion had increased to 39% (1).

Thyroid nodules harboring occult foci of PTC often go undetected, with up to a 35.6% prevalence in the general population at autopsy (7), far greater than the 1.1% prevalence of clinically apparent PTC (8). Presumably, the increasing incidence of PTC reflects the detection of previously undetectable PTC, which would have likely remained clinically unapparent for a person's lifetime if not for the increasingly widespread use of ultrasound

and technological advances in ultrasound resolution. This hypothesis is borne out by the observation that despite the rising incidence of PTC, mortality from PTC remains stable (1,5). In South Korea, geographic variance in PTC incidence is strongly associated with local rates of cancer screening – a national cancer screening program was initiated in 1999, and thyroid ultrasound is often added to the screening services for a small fee (5).

The current standard of care for thyroid cancer is immediate partial or total thyroidectomy (9). In the U.S., more than 90% of patients diagnosed with thyroid cancer undergo surgery as the primary oncologic intervention, and 85% of these patients undergo total thyroidectomy (1). Following surgical intervention, the prognosis for PTC is excellent (10).

The rates of recurrence-free survival, distant disease-free survival, and cause-specific survival are particularly high for PTMC (11). Although all large PTCs must at one point have been small PTCs, there is evidence of important biological differences between PTMC and PTC. There is a reduction in 10-year disease-free survival and cause-specific survival for PTMC in those that present with preoperative vocal cord paralysis (12) or clinically evident nodal metastases (13). However, in a cohort of patients with pathologically incidental PTMC after thyroid surgery for benign conditions, Ito et al found that only 2.2% developed recurrent disease (11). Similarly, PTMC incidentally detected by ultrasound and without high-risk features also showed an excellent prognosis postoperatively, with a 10-year lymph node recurrence-free survival rate, distant recurrence-free survival rate, and cause-specific survival rate of 99%, 100%, and 100%, respectively (11).

The traditional management approach of immediate thyroid surgery for PTMC is being reconsidered in light of the very low disease specific mortality, low rates of recurrence, and the potential for complications from surgery. The current treatment practices are arguably overly aggressive. Indeed, in a retrospective review, Davies et al reported that only 27% of thyroidectomies at a single institution were performed because of symptoms attributable to a neck mass (14). Thus, a significant percentage of thyroid surgeries may be unwarranted, raising the critical question of whether it is appropriate for clinicians to uniformly recommend surgical treatment for all patients diagnosed with thyroid carcinoma, particularly PTMC. Many cases of PTMC may not require surgery but rather could be managed through an active surveillance protocol, which involves serial imaging studies and thyroglobulin (Tg) measurements (15). Following a diagnosis of PTMC, a patient undergoing active surveillance is monitored for signs of disease progression; if progression is detected, then a decision to proceed to surgery can be made. In addition, if a patient decides that the psychological burden of not undergoing treatment is too overwhelming, then switching to a course of surgical therapy is appropriate. In this article, we first review the active surveillance management strategy and discuss the barriers to implementation in the U.S. Then, we discuss the potential role of a thyroid cancer management tool, the Thyroid Cancer Care Collaborative (TCCC) for active surveillance. The TCCC will help mobile patients keep records of their surveillance, such as ultrasound results and laboratory tests, and may help to ensure that patients are not lost to follow-up. Moreover, the TCCC contains tools for clinicians to help identify patients who are optimal candidates for active surveillance so that appropriate selection criteria are utilized on an individualized basis. Finally, the tracking

capabilities of the TCCC can help to ensure that patients under surveillance are not lost to follow-up.

ACTIVE SURVEILLANCE: A POTENTIALLY USEFUL AND COST-EFFECTIVE STRATEGY FOR MANAGING PTMC

Active surveillance, or delaying surgery in favor of observation with serial ultrasonography, is a promising treatment strategy for PTMC. Trials of active surveillance of asymptomatic PTMCs from Japan have revealed that nonsurgical management of PTMC is a safe and a more cost-effective long-term management option than immediate surgery with postsurgical surveillance (15–17). Active surveillance patients who showed signs of disease progression (e.g., tumor enlargement) could undergo surgery without increased risk of disease recurrence. In these studies, patients with biopsy-proven, asymptomatic PTMC were followed using serial ultrasonography, regular serum Tg measurements every 6 or 12 months, and chest radiography or computerized tomography (CT). Ito et al (16, 17) followed 340 patients and found that 15.9% of them had tumor enlargement ≥ 3 mm after 10-year follow-up (17). The cutoff for size enlargement was set at 3 mm because ± 2 mm was deemed to be the degree of error of ultrasound measurement and was, based on the authors' experience, within the range of observer variation. Additionally, metastases to cervical lymph nodes were observed in 1.4% and 3.45% of the cohort at the 5- and 10-year follow-ups, respectively. Sugitani et al (15) followed 230 patients and reported a similarly low rate of enlargement and nodal metastases: only 7% of PTMCs increased in size, only 1% of patients developed lymph node metastases, and no patients developed distant metastases or extrathyroidal invasion after a mean follow-up time of 11 years (15). Admittedly, these strategies will not pick up the rare patient that may have asymptomatic distant metastases at presentation or in the early course of surveillance. However, neither Ito et al nor Sugitani et al reported such patients in their cohorts (17,18).

This encouraging data suggests that the rate of growth of most primary PTMCs is slow and that the risks of tumor enlargement ≥ 3 mm and development of locoregional metastases while under observation is very low (15,17). On the basis of their results, Sugitani et al argue that 95% of patients with asymptomatic PTMCs are candidates for nonsurgical management (15). Two exceptions may be younger patients (19) and those who may become pregnant (20). Ito et al (19) report that age <40 years is an independent predictor of tumor growth in subclinical PTMCs. Shindo et al (20) compared 9 pregnant patients with PTMC and 27 age-matched control patients and found that PTMC enlargement was observed in 44% of the pregnant patients but only 11% of the controls, possibly due to the thyroid-stimulating activity of human chorionic gonadotropin. In addition to the low risk of disease progression, data from the Ito and Sugitani studies also suggest that patients may switch to surgery after detection of disease progression, as delayed surgery for PTMC is still associated with excellent outcomes and survival (15,17). It is important to note that even in the setting of larger PTC tumors, only a delay from diagnosis to therapy ≥ 12 months had an adverse effect on outcome, increasing the likelihood of cancer mortality by 130% (21).

The parameters for the decision to exit active surveillance and proceed to surgery must be clearly defined. Sugitani et al provided the option of conventional surgical therapy to all asymptomatic patients with PTMC (18). In both Japanese active surveillance studies (15–17), the patients were advised to undergo surgery if they met the following criteria during active surveillance: (1) a change in the patient's desire to remain under active surveillance, (2) tumor enlargement, (3) the appearance of clinically evident lymph node metastasis, and (4) tumor growth towards the dorsal surface of the thyroid gland or adjacent structures. The Ito and Sugitani trials differed slightly in that Ito et al (17) also recommended surgery for patients who were later diagnosed as having familial carcinoma, young age, suspicion of multicentricity, or the coexistence of other thyroid diseases (e.g., enlargement of associated benign nodules). Additional criteria may be considered: (1) suspicion of invasion of the recurrent laryngeal nerve (RLN) (e.g., the development of hoarseness or dysphagia), (2) the development of any other cancer-related symptoms, and (3) a new biopsy diagnosis that indicates higher grade malignancy. In future studies, these criteria may change, particularly with ongoing research on molecular markers, which may help identify tumors that are likely to grow.

Brito et al outlined a clinical framework for identifying patients who are ideal, appropriate, or inappropriate candidates for active surveillance (22), detailing the ultrasound characteristics, patient characteristics, and medical team characteristics necessary to successfully implement active surveillance protocols. Brito et al emphasized that factors such as the patient's comorbidities and the experience level of the medical team must be considered when selecting observation for PTMC patients.

One of the major benefits of active surveillance is that it avoids the risks associated with thyroid surgery. While postoperative RLN damage and transient or permanent hypoparathyroidism are infrequent, these complications can be clinically significant when present (23). The rate of permanent hypoparathyroidism is low (0.9% in 1 study), but the rate of transient hypocalcemia can be much higher (27.9% in the same study) (23). Bilateral vocal cord paralysis is observed in 0.2 to 0.5% of thyroidectomies but is a very significant complication (24). Thyroid lobectomy for small tumors is an accepted treatment option that avoids the risk of bilateral vocal cord paralysis, hypoparathyroidism and, in many cases, the need for thyroid hormone supplementation (9,25,26). For patients with small thyroid cancers located in the isthmus, without other nodules or adverse features, an isthmusectomy can be performed without virtually any surgical risk and under local anesthesia. Moreover, tumors in the isthmus appear to be more likely to manifest extrathyroidal extension (27). However, foregoing surgery altogether eliminates the risks associated with anesthesia and the cosmetic effect of a surgical scar.

CHALLENGES TO IMPLEMENTATION OF ACTIVE SURVEILLANCE PROTOCOLS

Clinical Factors

One challenge for active surveillance is to identify which patients have cancers that are likely to grow, spread to regional lymph nodes, and/or metastasize to distant sites. A size <1

cm does not guarantee indolence, and a PTMC could represent biologically aggressive disease. Thus, the widespread use of ultrasound may not only be responsible for the increased incidence of PTMC, but also the increased diagnosis of more biologically aggressive cancers at a much earlier stage. More aggressive PTMC may be identified on the basis of high-grade cytologic features or certain genetic mutations (e.g., the telomerase reverse transcriptase [*TERT*] promoter mutation, identified by Melo et al in 7.5% of PTCs in a review of 647 thyroid tumors) (28). However, there is currently no molecular profile that would either guarantee or predict that a PTMC will not progress. Furthermore, ultrasound and fine-needle aspiration biopsy (FNAB) findings used to make the diagnosis of thyroid cancer offer only a snapshot of the disease at a single moment, not its behavior over time. The ultrasound appearance may or may not be informative, and Sugitani et al reported that only the ultrasound feature of a rich blood supply to the PTMC tumor was predictive of future growth in size (15). Cappelli et al and Hong et al also found this feature to be predictive of unfavorable outcomes in PTMC (29,30).

Protocol Adherence

Active surveillance patients must be fully adherent to the protocol for tumor changes to be noted early so that action can be taken. Adherence to treatment is dependent on many factors including the patient's cognitive status, support in the home, and removal of barriers to obtaining medical treatment (31,32). Patients considering active surveillance need to be screened early for these factors. Data from active surveillance trials with prostate cancer patients in the U.S. suggests that compliance rates vary for different protocols. In the prospective Prostate Cancer Research International Active Surveillance (PRIAS) study of 4,547 men with low-risk prostate cancer followed with active surveillance, compliance with prostate-specific antigen (PSA) testing was high (91%) (33). Compliance with standard repeat biopsies decreased over time, from 81% at 1 year after diagnosis to 33% at 10 years after diagnosis. However, there are limitations in comparing active surveillance cohorts for prostate cancer with those for thyroid cancer. Prostate cancer mostly affects older males, while thyroid cancer patients tend to be middle-aged females. Moreover, prostate cancer surveillance can be more invasive than thyroid cancer surveillance, so it is not easy to generalize rates of compliance to active surveillance protocols between these populations.

Easy access to sonography and patient education are crucial components of an active surveillance management strategy for PTMC. Proper education of the patient may decrease cancer and surveillance-related stress, facilitate patient compliance with active surveillance protocols, and improve follow-up. Moreover, access to and optimal coordination of care are necessary for successful implementation of active surveillance as thyroid cancer is generally managed by multiple healthcare professionals (34) who may be at different institutions or locations with different record keeping formats and electronic health record applications.

Quality of Life

Patients must be carefully evaluated based on consideration of their quality of life, including their perceived tolerance of living with cancer. Thyroid cancer, its diagnosis, and its treatment introduce physiological and psychological stressors that may negatively impact a patient's quality of life (35). In a survey of 62 previously treated thyroid cancer patients,

Roberts et al found that overall quality of life was high; however, 38.8% of patients reported concerns about recurrence (36). Patients also reported unmet information needs after treatment. A recent larger study of 2,000 thyroid cancer patients reported similar high levels of unmet information and support needs, with only one-fifth of patients indicating that they received care and information about emotional and psychological concerns (37). The impact of a patient's perception of living with cancer as a chronic disease while undergoing active surveillance may be very different than a patient's perception of enduring long-term follow-up after successful surgical treatment (38), and psychological support may be even more necessary.

Psychological factors such as generalized anxiety and tolerance for uncertainty may also play roles in both the decision to choose active surveillance and continued adherence. While there is no data on the quality of life of active surveillance patients for thyroid cancer, the prostate cancer literature may be helpful. Lepore and Eton reviewed the literature on quality of life for prostate cancer patients and found that the diagnosis of and treatment for prostate cancer affected disease-specific health-related quality of life such as urinary, sexual, and bowel function, as well as general health-related quality of life (39). Despite the adverse effects of treatment on quality of life in prostate cancer patients, some surmise that active surveillance is underutilized as a result of expectations by clinicians that the protocol will cause adverse psychological effects. Indeed, patients undergoing active surveillance for both prostate and thyroid cancer have elected to switch into treatment groups based on anxiety (17,18,40). However, in a review of studies on prostate cancer patients undergoing active surveillance, Carter et al found that active surveillance did not pose a greater threat to psychological wellbeing than immediate treatment (41). Compared with patients undergoing immediate treatment, active surveillance patients had similar levels of anxiety, depression, emotional functioning, and quality of life. Moreover, Venderbos et al found that general anxiety and fear of disease progression decreased in active surveillance patients over time (42).

As noted above, it is important to recognize differences between thyroid and prostate cancer populations when translating quality of life data. Still, the information from prostate cancer active surveillance studies is encouraging for the implementation of active surveillance protocols to thyroid cancer management.

The Cultural Context

Patients' psychological response to active surveillance may be idiosyncratic and culture dependent (43). Despite the success of active surveillance in Japan, there are barriers to the implementation of active surveillance protocols in the U.S. (18). Sugitani and Fujimoto outlined several sociomedical differences between Western countries and Japan, where the longest active surveillance clinical trials have been based (18), which could impact the ability of active surveillance protocols to be translated effectively to Western countries. The first is the availability and acceptance of routine sonography. In Japan, thyroid ultrasonography is widely used, and surveillance ultrasounds are performed by surgeons rather than radiologists or technicians as in the U.S. and other Western countries (18). The quality and consistency of ultrasound for longitudinal evaluation of the thyroid and cervical

nodal basins is a significant factor in active surveillance and poses a challenge for the implementation of this type of program outside of high-volume thyroid centers.

As described above, a patient's willingness to adopt a strategy of lifetime surveillance is an important element. Both the Sugitani et al and Ito et al studies reported extremely low dropout rates of 3% and 0%, respectively (15,17). It is unclear whether inherent differences in the mobile nature of American citizens, especially younger individuals, will allow this strategy to be successfully adopted. Rates of patients being lost to follow-up are often high in the U.S. (44). Moreover, variations in practice patterns in thyroid cancer management have been reported in the U.S. (45).

In addition, medicolegal liability concerns may complicate efforts to implement active surveillance protocols in the U.S. and may influence a physician's recommendation for a patient who otherwise may be deemed to be a candidate (18). This may be particularly salient in cases where the physician believes a patient may not adhere to regular, lifetime surveillance. Other concerns such as a patient's ability to obtain life or disability insurance may also play a role in physician decision-making (46).

TCCC: A VEHICLE FOR ACTIVE SURVEILLANCE

These challenges highlight the importance of finding innovative solutions that will enhance the collection, analysis, and communication of clinically significant thyroid cancer information. Active surveillance would be optimized by utilizing a dynamic vehicle for maintaining patient clinical information that can be used by treating physicians regardless of the connectivity or commonality of their electronic health records. In this context, a model vehicle would serve not only as a clinical medical records support system, but also as a patient-physician communication system. Ideally, these functions would be seamlessly integrated to provide the ability to track patients and remind them of the need for follow-up visits.

In a review of population-based cancer registries, health systems-based cancer registries, and patient registries, Mehra et al discussed the benefits and limitations of different registry systems for thyroid cancer management and research (47). Mehra et al presented the TCCC as a patient registry that could address the limitations of population-based and health systems-based cancer registries, such as the challenge of patient-driven, long-term follow-up and dynamic data fields. The TCCC is a disease-specific electronic health record system accessible at no cost to patients and their self-selected team of care providers, regardless of institutional affiliation. By storing health data in a patient-centered way that is portable and accessible, the TCCC provides advantages over traditional electronic health records in facilitating active surveillance. In particular, the ability to track patients who may move or change physicians during the course of active surveillance can be enhanced by use of the TCCC. The TCCC is hosted in a Health Insurance Portability and Accountability Act-compliant environment on a secure server (hosting. com). While patients without computer or internet access are unable to use the TCCC themselves, they may still grant permission for their physicians to store and share their clinical information through the system.

The TCCC was developed to assist in the management of patients with thyroid cancer and includes modules that promote uniform evaluation of thyroid nodules and support uniform reporting of ultrasound findings. The Imaging and Cytology Module records 33 ultrasound parameters for thyroid nodules and cervical lymph nodes, including all parameters addressed in a multidisciplinary consensus statement on ultrasound reporting (Fig. 1A) (48). The Imaging and Cytology Module also includes other patient information such as family history of thyroid cancer or radiation exposure and FNAB results if the nodule was biopsied (Fig. 1B). For clinicians, this module allows comparison between serial exams at the time and location of decision-making. Moreover, these reports are available to any physician that becomes involved in the patient's care if the patient moves or changes care teams.

A clinical decision-making module in the TCCC assists clinicians in selecting patients who are optimally managed by observation based on the disease characteristics, the characteristics of the patient, and the characteristics of the medical team (Fig. 2). The TCCC records patient characteristics identified by Brito et al that are the most important factors in determining patient eligibility for active surveillance (22). This includes patient age, tumor size and location, and willingness to comply with lifelong follow-up. We are currently conducting research to add psychological variables to the TCCC that would help screen out patients who are unlikely to adhere to the treatment because of treatment anxiety or lack of support in the home. These characteristics can be entered into dedicated modules that can help to determine whether a patient meets the criteria for active surveillance (Fig. 2).

The TCCC currently collects and stores the following information for patients undergoing active surveillance:

- Patient age
- Size and borders of the primary tumor
- Tumor cytology
- Molecular profile of the primary tumor
- Tumor focality
- Location of tumors
- Presence of ultrasound features suggestive of extrathyroidal extension
- Tumor-related symptoms
- Status of the neck and distant sites
- Comorbid clinical conditions
- Family history of thyroid cancer
- Patient willingness to undergo active surveillance

If any parameters change, such as tumor growth, emergence of suspicious or biopsy-proven lymph nodes, or development of patient symptoms, these changes may be entered into the TCCC, which will provide information and recommendations to clinicians about the status

of the patient undergoing active surveillance. Moreover, the TCCC is updated regularly to present the most recent guidelines for active surveillance management.

In addition, the TCCC has a dedicated patient portal, allowing the patient themselves to become active participants in their care. Patients are given full access to their medical records and recommended follow-up procedures. The TCCC also serves as a patient education tool with an extensive educational video library, frequently asked questions page, and regular updates on current thyroid cancer research.

Finally, as active surveillance expands in practice, it will be important to evaluate its applicability in different medical settings and to monitor patients undergoing active surveillance over time. The TCCC may be used for research purposes as it collects data over a patient's lifetime.

RECOMMENDATIONS FOR ACTIVE SURVEILLANCE IMPLEMENTATION IN THE U.S

In order for active surveillance to be implemented in the U.S., there are several measures that must be considered.

First, it will be important for clinicians to develop systems to standardize thyroid ultrasounds and record keeping so that PTMCs can be tracked consistently over time. Moreover, clinicians must allow for adequate coordination of care among all healthcare professionals involved in a particular patient's active surveillance program.

Second, proper education of patients and clinicians is essential. Clinicians must be familiar with the active surveillance protocol and understand which factors would make a patient eligible or ineligible for continued active surveillance. Patients must understand their follow-up regimen so that, if a PTMC grows or other adverse features develop, it is detected and treated early.

Third, if a patient is deemed a good candidate for active surveillance from a clinical standpoint, he or she should be screened for other factors that could impact his or her adherence to the protocol, as active surveillance patients must be able to make regular appointments and comply with lifelong follow-up. Having a stable living situation, family or community support, and regular communication with clinicians are factors that may impact a patient's ability to comply with follow-up.

Fourth, patients should be screened for anxiety and tolerance for uncertainty before active surveillance is recommended. Moreover, psychological support should be offered to all patients choosing active surveillance to ensure that the patient is able to maintain a good quality of life.

Fifth, continued research will be required to monitor the success of active surveillance, as there are still several unanswered questions. For instance, what should be done for a patient who has a 9-mm PTMC that grows 2 mm to 1.1 cm? Will American patients comply with

the protocol to the same degree as Japanese patients? These questions and others should be investigated through research efforts and comprehensive patient monitoring.

CONCLUSION

With proper patient selection, organization, and patient support, active surveillance promises to be a safe and more cost-effective management strategy for selecting patients with PTMC. The potential impact of undergoing active surveillance on a patient's quality of life is emphasized, as well as the obligations of both the care team and the patient that are required to successfully implement this management strategy.

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Abbreviations

CT	computed tomography
PTC	papillary thyroid carcinoma
PTMC	papillary thyroid microcarcinoma
TCCC	Thyroid Cancer Care Collaborative

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Fig. 1. A, The Imaging and Cytology Module provides a visual representation of the thyroid, cervical lymph nodes, and other neck structures, along with detailed information about ultrasound characteristics and biopsy results.. B, The Imaging and Cytology Module records sonography and cytology results for thyroid nodules and tumors over time to allow easy identification of changes in size or sonographic features.

When to Perform Active Surveillance

1. Data Checklist

2. Critical Questions

3. Analysis

4. References

5. New Clinical Studies

This clinical decision-making module of the TCCC has been designed by physicians experienced in thyroid cancer care to assist physicians and patients in making the best decisions in their particular case. It cannot substitute in any way for the physician's clinical judgment. It is intended to only provide broad guidelines for when to perform a completion thyroidectomy, but the care of any particular patient is dependent upon a careful consideration of the many factors that are unique to that patient.

The optimal approach for a particular patient must be determined within the context of the patient's clinical presentation and course of past treatment. Management decisions should be reached only after a complete evaluation of all pertinent factors, and through direct discussions between the patient and their treating physicians, who are most familiar with the exact details of that patient's clinical history and clinical circumstances.

Categories	Clinical and Imaging Characteristics	Patient Characteristics	Medical Team Characteristics
Optimal for Active Surveillance	<ul style="list-style-type: none"> ✓ Surrounded by ≥ 2 mm normal thyroid parenchyma ✓ Previous US documenting stability ✓ cM0 ✓ Size of primary tumor <1cm 	<ul style="list-style-type: none"> ✓ Supportive significant others (including other members of their health care team) 	—
Acceptable for Active Surveillance, but Consider Surgery	<ul style="list-style-type: none"> ⚠ Multifocal papillary microcarcinomas ⚠ Ill-defined margins ⚠ Potentially aggressive molecular profile 	<ul style="list-style-type: none"> ⚠ Middle-aged Patient (18–59 yrs) ⚠ Child bearing potential 	—
Favor Surgery	<ul style="list-style-type: none"> ✗ Evidence of extrathyroidal extension ✗ N1 disease at initial evaluation or identified during follow-up 	<ul style="list-style-type: none"> ✗ Unlikely to be compliant with follow-up plans ✗ Not willing to accept an observation approach 	<ul style="list-style-type: none"> ✗ Reliable neck ultrasonography not available ✗ Little experience with thyroid cancer management

Fig. 2.

Active surveillance module assists physicians and patients with the decision as to which patients are optimal, acceptable, and not favorable candidates to undergo active surveillance.