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Active Surveillance of Low-Risk Thyroid Cancer

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In the past year, there were an estimated 53 990 new cases of thyroid cancer in the United States, representing a 3-fold increase in incidence during the past 3 decades.[1] While most of this increase has been attributed to sonographic detection of small, localized papillary thyroid cancers, there has been an increase in incidence of all stages of thyroid cancer.[2,3] Despite this increase in the number of individuals diagnosed with thyroid cancer, mortality has increased only slightly and has ranged from 0.4 to 0.5 per 100 000 people per year since 1980. Approximately 2060 people were estimated to die from thyroid cancer in the United States in 2018.[1]

Given the low risk of disease progression in many incidentally discovered papillary thyroid cancers, surgical excision may result in more harm than benefit. Even in the hands of the most experienced surgeons, thyroidectomy carries the risk of injury to the recurrent laryngeal nerve (about 1%) and parathyroid glands (0%-2%), as well as anesthetic-related complications. Many patients also develop a lifelong need for thyroid hormone replacement following surgery.

To address these concerns, in the early 1990s, 2 Japanese centers began offering serial ultrasonography surveillance in lieu of immediate surgery to patients with localized subcentimeter papillary thyroid carcinomas.[4,5] Extended follow-up demonstrated that the majority of these tumors remained unchanged or decreased in size compared with baseline measurements. When patients with tumors that exhibited growth or lymph node metastases underwent surgery, complete tumor and the metastatic lymph node excision was routinely achieved and none of these patients died from thyroid cancer. Similar "active surveillance" protocols have now been adopted by several US thyroid cancer programs for papillary thyroid nodules of up to 1.5 cm in diameter and are achieving outcomes that are equally favorable to the Japanese series.[6,7]

In longitudinal observational studies of patients with subcentimeter, biopsy-confirmed papillary thyroid cancer undergoing 10 years of active surveillance follow-up, 7% to 16% went on to require surgical intervention.[5,8] Four percent to 8% of the interventions were for nodule growth, 1% to 2% were for the development of cervical lymph node metastases, and 2% to 6% were for other reasons, including patient preference and the development of other thyroid or parathyroid disease. Tumor enlargement and/or the novel appearance of nodal metastases during follow-up were 5.6-fold more common in young patients (aged <40 years; 8.9%) vs older patients (aged ≥60 years; 1.6%).[8]

Consideration of active surveillance must be accompanied by an appropriate clinical framework consisting of ideal characteristics related to the patient, the tumor, and the health care system (**Box**).[9] Patients being considered for active surveillance should be older than 60 years and have availability for regular, long-term follow-up within their health system. Ideal tumor-related characteristics include the presence of only 1 low-risk thyroid cancer focus measuring 1 cm or less in greatest diameter and no evidence of extrathyroidal extension or nodal or distant metastatic disease. Tumors larger than 1 cm but less than 1.5 cm (T1bN0M0) appear to behave in a similar fashion as those measuring 1 cm or less (T1aN0M0).[10] Recommended health care system resources that are critical for such a consideration include a dedicated multidisciplinary team with experience in managing thyroid cancer, the ability to perform routine patient assessments longitudinally, the availability of high-quality ultrasonography and experienced operators, and a reliable follow-up system characterized by consistent patient tracking mechanisms and accurate reminders.[9] While most of the long-term follow-up data for active surveillance of thyroid cancer address nodules that are cytologically suspicious or diagnostic for papillary thyroid cancer, it is also reasonable to apply these same selection criteria to sonographically suspicious subcentimeter thyroid nodules that have not been biopsied.[7]

After a patient is enrolled in an active surveillance program, a reasonable approach is to assess the cytologically proven or, based on sonographic characteristics, highly probable thyroid cancer using ultrasonography every 6 months for the initial 2 years. If the size and sonographic characteristics of the tumor remain reassuringly unchanged during this period, it may be reasonable to

Box. Ideal Candidate and Health System Characteristics and Counseling Points for Patients Considering Active Surveillance for Thyroid Cancer

Candidate Characteristics[a]
- Solitary intrathyroidal papillary thyroid tumor ≤1.0 cm in greatest diameter, surrounded by 2 mm of normal thyroid parenchyma (ie, no local invasion)
- No suspicious lymph nodes
- No high-grade cytologic findings
- Age ≥60 years[b]
- Life-threatening comorbidities
- Committed to regular follow-up examinations

Health System Characteristics[a]
- Sophisticated patient tracking/reminders in the health record system
- Capability for high-quality neck ultrasonography
- Multidisciplinary team with experience managing thyroid cancer

Counseling Points
- Requires repeat ultrasonography examinations every 6 months to demonstrate stability, usually for 2 years, then every 1 to 2 years
- Approximately 15% of patients undergo surgery during long-term follow-up, usually for growth of primary thyroid tumor
- No significant morbidity or mortality associated with delayed surgical treatment of ideal candidates
- No head-to-head randomized trial data comparing surgery vs active surveillance

[a] Adopted from patient, tumor, and medical team characteristics of ideal candidates for observation described by Brito et al.[9]

[b] Younger patients are also reasonable candidates, realizing that progression to clinical disease is higher in younger age groups.

decrease the ultrasonography monitoring frequency to every 1 to 2 years or as clinical symptoms arise. Ultrasonography findings that should prompt consideration of a referral to thyroid surgery are (1) an increase in the greatest dimension of the thyroid nodule of at least 3 mm from the initial measurement and (2) new suspicious lymph node disease that is cytologically proven to be metastatic thyroid cancer. However, it has been suggested that 3-dimensional measurements of tumor volume showing more than a 50% increase is an early and accurate assessment of disease progression and suggests that tumor volume monitoring is useful.[6]

In the shared decision-making process of whether active surveillance might be a reasonable option for select situations, patients should be counseled that approximately 15% of individuals may ultimately undergo thyroid surgery during long-term monitoring, usually due to growth of the primary tumor.[5,8] Individuals should also be aware that there are currently no head-to-head randomized trials that compared active surveillance of low-risk thyroid cancer with thyroid surgery, and that there remain uncertainties related to the risks and benefits of each approach.

While active surveillance of small intrathyroidal thyroid cancers has the potential to reduce morbidity from surgical treatment, adoption of this strategy in the United States is in the early stages, and it remains unknown whether the favorable outcomes reported by specialized centers will be widely reproducible. Hopefully, future advances in molecular diagnostic testing of fine-needle aspiration material will aid patient selection by identifying the minority of thyroid cancers that will aggressively grow and spread without surgical excision. Until then, standardized mechanisms for evaluating individual preferences and risk tolerance for different treatment-related complications are needed to help patients decide between immediate surgery and observation of low-risk thyroid cancer.

ARTICLE INFORMATION

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