



Active surveillance for low risk papillary thyroid cancer

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We read with interest the article published by Akira Miyauchi, “Clinical Trials of Active Surveillance of Papillary Microcarcinoma of Thyroid” in the *World Journal of Surgery* [2016] (1), which summarizes 22 years of experience with this approach. Dr. Miyauchi, who is the father of active surveillance (AS) for low risk thyroid cancer, concludes that, “although we still offer two options, immediate surgery or observation, to patients with low risk papillary microcarcinoma (PMC) at Kuma Hospital, we now strongly recommend observation as the best choice.” The strong recommendation for AS over immediate surgery is based on the finding that the two approaches have similar oncologic outcomes; however, immediate surgery exposes patients to a low but measurable incidence of unfavorable events, such as vocal cord paralysis and hypoparathyroidism.

The concept of AS for low risk papillary thyroid cancer (LR-PTC) has been around since Dr. Miyauchi proposed the first trial in 1993; however, it only recently gained acceptance in US, marked by the publication of the American Thyroid Association (ATA) 2015 guidelines endorsing this approach (2). These guidelines were perhaps behind the times, as Japanese guidelines had endorsed AS as early as 2010. The recent ATA guideline endorsement was based on the same cohort data, updated now with data from Japan and South Korea (3-5). In these trials, patients with LR-PTC were offered a choice of AS and immediate surgery based on the tumor characteristics, reserving surgery for patients that showed tumor progression on follow-up. It is important to note that not all patients with small PTC are “low-risk”. Patients with regional or distant metastasis, extrathyroidal extension, high grade histology, and/or tumors with risk of tracheal or recurrent laryngeal

nerve invasion should be identified and offered upfront surgery. The review article also nicely outlines the clinical significance of tumor to trachea angle in posteriorly located tumors (obtuse angle has higher risk than others for tracheal invasion) and rim of normal thyroid tissue between the tumor and recurrent laryngeal nerve (RLN), and its relevance in the decision-making process. These patient-selection factors highlight the importance of expert radiological consultation for success of this management strategy.

In the Kuma hospital cohort, after 10 years of observation, only 8% of patients had tumor progression as measured by size enlargement of >3 mm, and only 3.8% patients had a novel node metastasis. Importantly, rescue surgery for these patients with tumor progression was successful. No one in either the immediate surgery or active surveillance groups, including those patients needing later surgery, died of thyroid cancer. Further, complications and cost of treatment was significantly lower in the AS group compared to the immediate surgery arm. Another interesting observation is that stratifying patients as young (<40 years), middle age (40–60 years) and old (>60 years) predicts the likelihood of disease progression, with younger patients choosing AS being more likely to eventually require surgery.

Our own experience at MSKCC has shown that a similar management strategy of AS is not only feasible in the United States, but has similar results (6). In addition to tumor progression as measured by novel nodal metastases and diameter increase of the tumor >3 mm, we also assessed tumor volume, and found it to be an earlier predictor of tumor growth than 3 mm diameter increase. Also, we included patients with tumors up to 1.5 cm; patients with

tumors larger than 1cm showed similar outcomes to smaller tumors. Clinical risk stratification was important in the MSKCC cohort as well; patients were classified as ideal, appropriate or inappropriate for AS, based not only on ultrasonographic features, but also on patient characteristics and medical team characteristics (7).

While the findings summarized in the article by Miyauchi have been proposed before, to see the conclusion in writing that physicians should favor one strategy over another for low risk PMC is certainly novel. By definition, the patient's choice for immediate surgery or AS is a "preference-sensitive" one, where there may be unique benefits and harms to either approach. For instance, it is important to realize the psychological impact of cancer diagnosis on an individual. Health utility studies in patients undergoing AS for low risk prostate cancer have shown that the mere diagnosis of cancer reduces the well-being of patients (8). Therefore, appropriate shared decision-making requires at least that the two strategies be discussed and offered, and the benefits and harms weighed, in the context of a patient's preferences and values.

In clinical scenarios, after such a discussion with a patient, many patients might ask, "Well, what would you do if it were you, or your family member?" Today, Dr. Miyauchi has made it known what he would say. While others may not yet agree with him, certainly some do. In the future, undoubtedly, many more clinicians will also favor AS for their well-selected patients. More research of course is required to identify appropriate patients and surveillance strategies, and assess long-term oncologic and patient-reported outcomes for those who choose AS.

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Footnote

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