Editorial

The role of active surveillance in low-risk papillary thyroid carcinoma

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Incidence of thyroid carcinoma has increased by 2- to 3-fold in many countries in the last years, reaching an epidemic 15-fold increase in Korea (1-3). The vast majority is represented by newly diagnosed thyroid papillary microcarcinoma [<10 mm, micropapillary thyroid carcinoma (mPTC)], which has probably risen because of earlier and more accurate screening programs (1-4). The natural history of mPTC is anyway quite indolent and only a small proportion of pMTCs show a progression requiring surgery (4,5). In a recent study by Ito *et al*., mPTC progression has been demonstrated to be inversely related to patient's age (4). Data showed evolution of mPTC during a 10-year follow-up within the younger population (<40 years) of patients observed when compared to the older one (>60 years), regarding size enlargement (P=0.0014), lymph nodes metastases appearance (P<0.0001) and progression to clinical disease (P<0.0001) (4). The author recommends active surveillance in patients with low-risk mPTC (papillary microcarcinoma without clinically evident metastases or local invasion, and no convincing cytologic evidence of aggressive disease) especially when old (age >60 years), avoiding thus immediate surgery (4). Active surveillance is a treatment plan that consists in closely following a patient by means of exams and tests done on a regular schedule, not giving any treatment unless the condition observed shows progression. It may be used to avoid or delay treatments such as surgery thus reducing or completely skipping treatment-related complications (4-6). Active surveillance has been also advised by the last American Thyroid Association (ATA) Guidelines as a safe possible alternative to immediate surgery in low-risk mPTC patients (5). However, it is of outmost importance to emphasize that a careful selection and follow-up of patients is the key factor for active surveillance and it should be pursued following a well-designed prospective clinical trial, in order to resolve any problems and question encountered during it (6). Although small mPTCs still have the potential to harm patient's life. A surveillance, epidemiology and end results (SEER)-based analysis of Nilubol *et al*. reports that among all patients died for thyroid cancer in the US between 1988 and 2007, 7.7% have been diagnosed with a previous mPTC (7).

The recent paper of Oda *et al*. from the group of Kuma, Japan, answer many questions regarding the role, the potential and maybe the pitfall of active surveillance of mPTC, not only from an oncological standpoint, but also investigating surgical complications associated to immediate or delayed surgery (8). This large prospective trial enrolled overall 2,153 patients, with a median follow-up of 47 months (range, 12–116 months). Of these, 1,179 patients chose active surveillance while 974 patients preferred immediate surgery. In the active surveillance group, only 94 patients (8.0%) underwent surgery for tumor enlargement or novel lymph nodes metastases. None of the patients presented during follow-up distant metastases, and none died of the disease (8). On the other hand, immediate surgery group reported a higher morbidity concerning transient vocal cord palsy (4.1% *vs*. 0.6%, P<0.0001), transient and permanent hypoparathyroidism (16.7% *vs*. 2.8%, P<0.0001 and 1.6% *vs*. 0.1%, P<0.0001). Moreover, the proportion of patients under L-thyroxine supplementation or thyrotropin (TSH)-suppressive therapy was also reported to be higher in the immediate surgery group than in active surveillance group (66.1% *vs*. 20.7%, P<0.0001), as well as incidence of post-surgical hematoma and surgical neck scar (0.5%

Table 1 Comparison of unfavorable events between active surveillance, delayed and immediate surgery

Variables	Active surveillance	Delayed surgery	Immediate surgery	P value
Patients (n)	1,179	94	974	–
tVCP [n (%)]	7 (0.6)	7 (7.4)	40 (4.1)	<0.0001
tHypo [n (%)]	33 (2.8)	33 (35.1)	163 (16.7)	<0.0001
pHypo [n (%)]	1 (0.1)	1 (1.1)	16 (1.6)	<0.0001
Hematoma [n (%)]	0 (0.0)	0 (0.0)	5 (0.5)	<0.05 (active surveillance *vs*. immediate surgery)
Neck scar [n (%)]	94 (8.0)	94 (100.0)	974 (100.0)	<0.0001 (active surveillance *vs*. immediate surgery)
Recurrence [n (%)]	1 (0.1)	1 (1.1)	5 (0.5)	ns
Death*	3	3	5	ns

*, death was always not related to thyroid cancer. ns, not significant; tVCP, temporary vocal cord palsy; tHypo, temporary hypoparathyroidism; pHypo, permanent hypoparathyroidism.

vs. 0.0%, P<0.05 and 100.0% *vs*. 8.0%, P<0.0001) (8). The oncological outcomes were equally excellent between the two groups (P=ns) allowing the authors to conclude that, given an increased incidence of unfavorable events in the immediate surgery group, active surveillance is now recommended as the treatment of choice for low-risk mPTCs (8).

Oda *et al*. performed a robust, valuable and well-designed study. The follow-up offered in the facility of Kuma was precise and efficient and allowed to achieve a very strong statement which should influence the management of patients diagnosed with mPTCs. Nevertheless, some points need to be discussed. Temporary vocal cord palsy (tVCP), temporary (tHypo) and permanent (pHypo) hypoparathyroidism, neck scar and post-surgical hematoma were more frequent when comparing the whole numbers of patients (1,174 active surveillance group *vs*. 974 immediate surgery group). If we extrapolate data and finally compare those variables between the 94 delayed surgery group and the 974 immediate surgery group, it seemed that a higher complication rate occurred in the delayed surgery group (see *Table 1*). This could be explained, by the fact that when conversion from surveillance to surgery was made, the lesion was larger and lymph nodes metastases were present, thus, although operating with the same technique (hemithyroidectomy plus tracheal dissection or total thyroidectomy plus neck dissection), overall transient parathyroid and laryngeal nerve morbidity raised to 35.1% and 7.4% respectively. Although cervical neck scar is reported to be statistically different between the two groups of the study (*Table 1*), this specific parameter is not univocally accepted as a criterion. Neck scar actually is mainly a cultural issue concerning almost all the population in Eastern countries (especially Korea and Japan) while is not considered a surgical complication in Western countries, unless the development of a cheloid scar. So far, its use to reinforce statistical analysis may lack interest when evaluating European or US population. Interestingly, Oda *et al*. evaluated also the emotional status of patients when choosing the medical option, reporting a good compliance and acceptance when correctly informed by the surgeon. This is an important issue that is underevaluated: quality of life of patients. There is no randomized study in literature evaluating the quality of life in patients followed by active surveillance *vs*. immediate surgery. Such a study, performed by means of specific measurement tools (SF-36, WHOQOL-Bref or others) would be useful to help physicians and patients to choose the best medical option. Nevertheless, it could be a difficult study for the need of a prolonged (sometimes up to 10–15 years) follow-up, considering the quite indolent course of mPTC.

To conclude, the results of Oda *et al*. are of extreme interest and should be taken into account by surgeons when managing patients with mPTCs. Low-risk mPTC may benefit from a non-surgical approach. The approach of active surveillance should be tailored regarding both pathological and cultural status of the population concerned. Clear and comprehensive information to patients is one of the key to manage the emotional aspects associated to a diagnosis of cancer (8).

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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