Editorial

Comments on *National guidelines for diagnosis and treatment of thyroid cancer 2022 in China (English version)*

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Thyroid cancer (TC) is the most common endocrine system cancer, of note, the overall survival of TC in China is suboptimal when comparing with the developed countries such as US (84.3% *vs.* 98.3%), posing a great challenge among professionals involved in this field. Standardization of its diagnosis and treatment not only provides the basis for all the care givers to promote the entire level of TC management, but also is helpful in shortening the distance between China and other developed countries. A multidisciplinary team (MDT) should be involved in the comprehensive clinical management of TC, particularly for those advanced or refractory TC, which needs cooperation among members from ultrasonography, radiology, pathology, surgery, nuclear medicine, external radiation therapy as well as oncology, and so on. Under the leadership of Chinese National Health Commission of the People's Republic of China, MDT experts have been organized to form the panel for this guidelines on TC with MDT perspectives based on latest relevant literatures. Comparing with other contemporary guidelines, guidelines herein covered almost all the different types of thyroid carcinoma, including differentiated TC (DTC), medullary TC (MTC), and anaplastic thyroid carcinomas (ATC), which account for more than 98% of the whole pathological spectrum of TC and provided recommendations for management of TC such as diagnosis and treatment from surgery, nuclear medicine and endocrinology, as well as comprehensive management for life-threatening refractory TC.

Screening and diagnosis of TC

Mass screening for TC in general population is not routinely recommended. High-risk factors were emphasized, including history of neck radiation exposure during early childhood, history of head and neck radiation therapy, and family history of TC or TC-related genetic syndromes. Groups with high risks should have their thyroid checked regularly (1).

For the diagnosis of TC, ultrasound-guided fine-needle aspiration cytology (FNAc) is the predominant preoperative histological means of confirmative diagnosis. Especially in the condition of increasing incidence of papillary thyroid microcarcinoma cancer (PTMC), FNAc

can avoid diagnostic treatment and optimize the benefit of patients (1).

Ultrasound and contrast-enhanced computer tomography (CT) are important examinations to assess the extent of lesions, while magnetic resonance imaging (MRI) and other examinations can be used as complementary means. Even for PTMC, the number and location of the primary focus as well as the central compartment and lateral neck lymph nodes should be carefully evaluated by ultrasound and enhanced CT. Assessment of vocal cords should be a routine examination. If invasions of trachea and/or esophagus are suspected, bronchoscopy and gastroscopy should also be performed (1,2).

^{18}FDG positron emission tomography-CT (PET-CT) is not routinely recommended for diagnosis, but may provide additional information upon clinical settings in the following conditions: 1) DTC patients with suspicious biochemical recurrence suggested by elevated serum Tg but negative radioactive iodine (RAI) imaging and 2) advanced DTC, MTC or ATC pre-treatment evaluation and staging, as well as evaluation for postoperative MTC with suspicious biochemical recurrence suggested by elevated calcitonin (1).

Surgical treatment of TC

Surgical treatment is the primary radical treatment for most thyroid cancers (1). Radical treatment is advocated even though most of DTCs carry a good prognosis. A comprehensive assessment of patients' gender, age, clinical stage, and comorbidities is needed to determine the appropriate extent of resection (1,3). PTMC does not equal to early-stage cancer and not all PTMC can be managed conservatively (4,5).

The scope of surgical resection for MTC should be more aggressive. Calcitonin and carcinoembryonic antigen as well as tumor markers are also informative in determining the appropriate extent of resection (6,7). Only a minority of ATC patients have the chances for surgical resection (8). However, with the advancement of systemic therapeutic agents, those who respond well to neoadjuvant therapy may be converted from inoperable to operable (9-11).

^{131}I therapy and thyroid stimulating hormone (TSH) suppression therapy for DTC

Apart from surgery, ^{131}I therapy and TSH suppression therapy are also crucial for TC (12-14). ^{131}I therapy should be managed on a comprehensive pre-RAI evaluation, which incorporating the American Joint Committee on Cancer (AJCC)/TNM staging, risk stratification, and dynamic response into therapy restaging system, and patients' preference and values towards the treatment should also be integrated (15-20). The goals of RAI therapy can be clarified into remnant ablation, adjuvant therapy and RAI therapy for persistence or metastases. Besides, the indications and administered activities of RAI therapy are also recommended accordingly. Since the optimal degree of TSH suppression varies among different patients, an individually tailoring for TSH targets is suggested after balancing the risk of side effects and benefits.

Refractory TC

RAI-refractory DTC (RAIR-DTC) means a status of RAI resistance and de-differentiation, and it constitutes the major part of life-threatening TC together with advanced MTC and ATC. Active surveillance and MDT cooperative management are recommended for these refractory TCs.

External beam radiation radiotherapy (EBRT) is not a routine treatment for DTC (1). The indications include unresectable lesions and R2 resected lesions whose progressions cannot be controlled by RAI (1,21). In MTC, EBRT can increase the local control rate for unresectable lesions and prominent extranodular extensions (22). For ATC, EBRT can be applied preoperatively or postoperatively as part of the multidisciplinary treatment, or alone or for palliative therapy to alleviate the symptoms (23).

Targeted therapy was considered for progressive or symptomatic RAIR-DTC patients, particularly when both surgery and RAI therapy fail to control the disease, we also emphasize the need to strictly tailor the indications. Multi-targeted kinase inhibitors, including lenvatinib, sorafenib and anlotinib, have been approved for progressive RAIR-DTC, and anlotinib for advanced MTC in China (24-26). For locally advanced unresectable TC, the neoadjuvant application of targeted therapy may create a new opportunity for surgery (9,27). Chemotherapy is rarely an option for DTC and MTC, but has an important role in ATC (1,28). An MDT cooperation is helpful in the response to systemic therapy assessment as well as the comprehensive management of adverse events.

It should be noted that rapid progress has been made in the field of TC, and new evidence of evidence-based medicine keeps emerging. Due to the given period of time

of the guidelines, many new research evidences have not been included timely, and the 2023 version with updated evidence can be expected.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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