

# Clinical Value and Indications of $^{131}\text{I}$ Treatment after Surgery for Differentiated Thyroid Cancer

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According to statistics, thyroid cancer is the malignant tumor with the fastest growing morbidity over the past 20 years, especially in females and young people [1,2]. Differentiated thyroid cancer (DTC) accounts for most cases of thyroid cancer, and is divided mainly into papillary and follicular thyroid carcinomas. Its prognosis is good, but recurrence and metastasis can occur in some patients [3].

The combination of surgery, iodine $^{131}$  ( $^{131}\text{I}$ ) therapy, and thyroid hormone treatment is an effective and acceptable therapeutic scheme for most DTC patients [4]. The first step in DTC treatment involves resection of the tumor and the affected thyroid tissue. Total resection or subtotal resection of the thyroid is preferred, to better prepare for postoperative  $^{131}\text{I}$  treatment, to improve the curative effect, and to reduce recurrence. However, total resection is rarely adopted, because of the risk of complications, and postoperative  $^{131}\text{I}$  treatment is therefore necessary.  $^{131}\text{I}$  treatment has two major purposes: ablating the residual thyroid cancer cells and treating DTC metastases.

There are several clinical reasons for using  $^{131}\text{I}$  treatment to ablate residual tumor tissues after DTC surgery. (1)  $^{131}\text{I}$  treatment can completely ablate very small tumor foci that may be hidden in the residual thyroid tissue after surgery, thus reducing local relapse. (2) After complete removal of the residual thyroid gland, serum thyroglobulin (Tg) becomes a sensitive tumor marker for monitoring recurrence and metastases after DTC surgery.  $^{131}\text{I}$  treatment thus improves the sensitivity of Tg as an indicator of recurrence and metastases, making it useful for long-term follow-up. (3) Ablation of residual thyroid tissue eliminates its competition for  $^{131}\text{I}$  intake, thus increasing  $^{131}\text{I}$  uptake by metastases and improving the sensitivity of  $^{131}\text{I}$  whole-body scanning for the detection of metastases.

Metastasis of papillary thyroid carcinoma mainly involves the lymph nodes, while metastases of follicular thyroid carcinoma involve the lungs and bone.  $^{131}\text{I}$  treatment of lymph node metastasis is mainly targeted at metastatic lymph nodes smaller than 1 cm, with good  $^{131}\text{I}$  intake, and favorable therapeutic effects can be achieved after repeated  $^{131}\text{I}$  treatment. Repeated  $^{131}\text{I}$  treatment of lung metastasis from DTC results in the reduction or disappearance of foci in most patients, and partial or complete alleviation of symptoms. The main effect of  $^{131}\text{I}$  treatment of bone metastasis is in alleviating pain; it can relieve or eliminate bone pain in most patients. At the same time,  $^{131}\text{I}$  treatment can also enable biochemical relief, reducing serum levels of the tumor marker Tg [5]. Apart from using  $^{131}\text{I}$  to treat metastases,  $^{131}\text{I}$  whole-body scanning can also be used to detect and qualitatively analyze new metastases.  $^{131}\text{I}$  thus has dual functions of diagnosis and treatment in relation to DTC metastases.

The decision to administer  $^{131}\text{I}$  treatment after DTC surgery should depend on the risks of relapse and death. I support the ESMO Clinical Practice Guidelines and European Consensus that classifies the risk of DTC as high, low, or extremely low. High-risk patients are those with tumors > 4 cm, with extraglandular invasions, lymph node and distant metastases, or with incompletely resected tumors. Low-risk patients refer to those whose thyroid glands were incompletely resected and who did not receive lymph node dissection, those with a tumor diameter

of 1-4 cm, adolescent patients, or those with invasive pathological manifestations. Extremely-low-risk patients are those with a single focus without extraglandular invasions, with no lymph node, or distant metastases, no invasive pathological manifestations, a tumor diameter < 1 cm, or whose thyroid gland was completely resected [6,7].

It is generally believed that high-risk DTC patients should receive postoperative  $^{131}\text{I}$  treatment, while extremely-low-risk patients do not require  $^{131}\text{I}$  treatment. However, the need for postoperative  $^{131}\text{I}$  treatment in low-risk patients is controversial. Indeed, the highly influential 'New England Journal of Medicine' recently published two randomized, multicenter clinical studies of postoperative  $^{131}\text{I}$  treatment in low-risk DTC [8,9]; a comparison and assessment of the therapeutic effects of low- and high-dose  $^{131}\text{I}$  (30 mCi and 100 mCi, respectively). With respect to the ablation of residual tissue and reductions in serum Tg, low-dose  $^{131}\text{I}$  treatment was comparable to high-dose  $^{131}\text{I}$  treatment. The incidence of adverse events, however, was significantly lower in patients treated with low-dose  $^{131}\text{I}$ , providing convincing evidence-based support for the use of  $^{131}\text{I}$  treatment in low-risk DTC patients. However, it is important to balance the advantages and disadvantages of  $^{131}\text{I}$  treatment in low-risk DTC patients. Low-dose  $^{131}\text{I}$  treatment is associated with a lower incidence of adverse events, with no change in therapeutic effect, and is therefore recommended in low-risk DTC patients. The prognosis of low-risk DTC is good and patients can survive for prolonged periods, highlighting the importance of long-term follow-up visits. The value of the tumor marker Tg is increased after  $^{131}\text{I}$  treatment, and can thus be used for long-term and life-long follow-up of low-risk patients. I therefore recommend that all DTC patients, except those classified as extremely low-risk, should receive  $^{131}\text{I}$  treatment after thyroid gland resection.

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