

## 分化型甲状腺癌<sup>131</sup>I治疗的争议与探索

### Controversy and exploration of <sup>131</sup>I therapy for differentiated thyroid cancer

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·述评·

# 分化型甲状腺癌<sup>131</sup>I治疗的争议与探索

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**【摘要】** 分化型甲状腺癌(DTC)患者在规范的手术、选择性<sup>131</sup>I治疗、TSH抑制治疗下多数预后良好。<sup>131</sup>I治疗目标分为清甲治疗、辅助治疗及清灶治疗,其可完善疾病分期、便于随诊、降低疾病复发及死亡风险,但临床实践中仍在存诸多待明确的问题,如术后<sup>131</sup>I治疗前评估中,亚临床病灶判断困难,且无用以指导治疗的Tg临界值,增加了辅助治疗的决策难度;治疗后随诊中,尚无评价结构性病灶<sup>131</sup>I治疗疗效的标准;TgAb的存在会影响病情判断;<sup>131</sup>I累积剂量相关并发症亦需监测管理。本期重点号刊登了数篇DTC患者<sup>131</sup>I治疗相关的文章,多方位讨论了当下<sup>131</sup>I治疗中的难点和我国学者的探索。

**【关键词】** 分化型甲状腺癌; 碘放射性同位素; 近距离放射疗法; 争议

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## Controversy and exploration of <sup>131</sup>I therapy for differentiated thyroid cancer

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**【Abstract】** Differentiated thyroid cancer (DTC) patients always holds a good prognosis under standard surgery, selective <sup>131</sup>I therapy and TSH suppression therapy. The goals of <sup>131</sup>I therapy are characterized as remnant ablation, adjuvant treatment, and treatment of known disease, which are supposed to refine initial staging, facilitate follow-up, decrease recurrence, and improve disease-specific survival. However, there are still many issues to be clarified in clinical practice. For example, in the assessment of postoperative disease status before <sup>131</sup>I therapy, it is difficult to estimate subclinical lesions, and there is no Tg threshold to guide <sup>131</sup>I therapy, which makes the decision of adjuvant treatment even harder. In the follow-up, there is no uniform response criterion for <sup>131</sup>I therapy in structural disease, the presence of TgAb will interfere with the judgement of disease status; <sup>131</sup>I cumulative dose-related complications also need to be monitored and managed. This issue contains several articles related to the <sup>131</sup>I treatment of DTC patients, discusses the difficulties in current <sup>131</sup>I treatment and the explorations of Chinese scholars in several aspects.

**【Key words】** Differentiated thyroid cancer; Iodine radioisotopes; Brachytherapy; Controversies

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甲状腺癌是内分泌系统最常见的恶性肿瘤,其发病率在世界范围内呈逐年上升趋势,2016年我国甲状腺癌新发病例数高达20.3万,约占全球甲状腺癌新发病例总数的1/3以上,远高于我国人口总数的全球占比(约18%)<sup>[1-3]</sup>。起源于甲状腺滤

泡细胞的DTC占甲状腺癌的90%以上,其保留了滤泡上皮细胞的部分分化特征,如特异性摄碘、依赖于TSH生长等。受益于其独特的生理特性,DTC患者在规范的手术、选择性<sup>131</sup>I治疗、TSH抑制治疗的经典综合管理下多数预后良好,在高发病率背

景下,病死率仍一直维持在较低水平。甲状腺癌好发于20~50岁人群,是威胁生产人群健康的主要疾病之一;此类基数庞大的患者需要终身监测疾病可能的复发、转移,极大增加了我国医疗负担。因此,完善甲状腺癌的相关管理,是提高我国国民健康水平、优化卫生决策的重要内容。

$^{131}\text{I}$ 治疗是DTC患者术后综合治疗的主要手段之一,其能够有效降低患者复发及死亡风险。依据TNM分期、疾病复发风险分层以实时的疾病状态评估结果, $^{131}\text{I}$ 治疗的目标可分为清甲治疗(清除手术残留的甲状腺组织以便随访监测与疾病再分期)、辅助治疗(探测并清除术后潜在的微小残留病灶,以降低复发及肿瘤相关死亡风险)与清灶治疗(治疗无法手术切除的局部或远处转移病灶,以改善疾病相关生存率及无病生存率)<sup>[4]</sup>。值得一提的是, $^{131}\text{I}$ 治疗的三种目标是人为区分的结果,在临床实践中,三者并非彼此独立,有彼此重叠的可能<sup>[5]</sup>。本期重点号中,敬凤连等<sup>[6]</sup>在回顾性探讨清甲效果的影响因素时同时入组了清甲、辅助、清灶三种治疗目标的患者,就是辅助及清灶剂量的 $^{131}\text{I}$ 兼具清甲效用的巧妙证明,该研究发现 $^{131}\text{I}$ 剂量高、甲状腺全切或近全切及治疗前TSH水平高的患者,首次清甲成功率高。

现行的 $^{131}\text{I}$ 治疗前评估理念强调了将TNM分期、复发危险分层与当下疾病状态有机结合,但其仍存在诸多亟待明确的问题。如辅助治疗的对象为亚临床残留和(或)复发和(或)转移性病灶,这种隐匿性病灶无法在影像学上被证实,因而治疗适应证的把握较为困难。2019年,马提尼克联合声明中亦指出,辅助治疗的决策不仅要全面考量疾病状态,平衡风险与获益,还要结合患者意愿及现有的医疗条件<sup>[5]</sup>。对评判术后残余甲状腺组织及疾病状态而言,甲状腺球蛋白(thyroglobulin, Tg)测定可作为一项灵敏便捷的指标,然而目前尚无明确的Tg临界值能够用以指导中高危患者辅助和(或)清灶治疗剂量的选择及预测疗效。本期重点号中,张潇宇等<sup>[7]</sup>着眼于无远处转移的中高危人群,回顾性分析并发现中高危DTC患者 $^{131}\text{I}$ 治疗前刺激性Tg水平是评价预后的独立影响因素,刺激性Tg水平 $<5.9\text{ ng/ml}$ 时更容易达到疗效满意(ER),为中高危人群的治疗指征及预后预测提供了一定参考。

$^{131}\text{I}$ 治疗后,患者复发风险及病死率可因干预

而变化,目前DTC患者长期随访中采用2015年美国甲状腺协会提出的治疗反应评估体系<sup>[4]</sup>来进行实时评估。虽然以疗效满意、生化疗效不佳(BIR)、结构性疗效不佳(SIR)、疗效不确切(IDR)四类反应可以有效区分不同临床转归患者,但存在结构性疗效不佳患者常终身带瘤生存,难以向其他三类转归,对其疗效的评价尚无统一标准,终止和(或)继续碘治疗的考量及碘难治性的判断受医师主观影响较大。2021年发布的四学会联合声明中提到,此类患者的疗效判断可将形态学肿瘤负荷、肿瘤代谢体积、Tg变化相结合<sup>[8]</sup>。本期重点号中,李娇等<sup>[9]</sup>深入探讨肺转移性DTC患者第1、2次 $^{131}\text{I}$ 治疗前刺激性Tg与TSH水平的动态变化对于临床转归的预测价值,发现以结构影像学病灶大小变化为标准,两次刺激性Tg与TSH水平比值的变化率、病理学类型及初始肺转移灶大小是预测肺转移性DTC进展的独立风险因子。

Tg作为DTC特异的肿瘤标志物,在DTC全程管理中具备无可替代的价值,然而其水平不仅受肿瘤负荷影响,还与TSH水平及抗甲状腺球蛋白(thyroglobulin antibody, TgAb)水平息息相关。TgAb阳性时,Tg水平检测会出现较大偏差,此时TgAb可作为替补肿瘤标志物。本期重点号中,韩娜等<sup>[10]</sup>探究 $^{131}\text{I}$ 治疗前TgAb阳性( $\geq 40\text{ IU/ml}$ )的DTC患者在 $^{131}\text{I}$ 治疗后TgAb转阴时间与临床转归的关系,发现TgAb转阴时间和 $^{131}\text{I}$ 治疗总剂量是影响临床转归的独立危险因素,在一定程度上亦提示了其作为替代肿瘤标志物的价值。

尽管临床实践已证实 $^{131}\text{I}$ 是一种有效且安全的治疗手段,但其仍存在诸多与累积剂量相关的早期及晚期并发症,累及消化、血液、生殖等多系统,其继发性恶性肿瘤的风险亦会有所增加<sup>[11]</sup>。唾液腺损伤是 $^{131}\text{I}$ 治疗最常见的并发症,由其造成的口干、腮腺肿痛、味觉改变等症状对患者的生活质量造成一定影响。本期重点号中秦洋洋等<sup>[12]</sup>、仝慧敏等<sup>[13]</sup>分别就 $^{131}\text{I}$ 治疗引起的唾液腺功能损伤的机制、症状、诊断及防治措施进行综述,为 $^{131}\text{I}$ 治疗引起的唾液腺损伤管理提供参考。

$^{131}\text{I}$ 治疗在DTC诊治中的独特价值已经经过80余年的临床验证。在简单的应用原理背后,从诊断到治疗,从初治到随访,临床实践中仍存在诸多悬而未决的问题。本重点号围绕 $^{131}\text{I}$ 治疗DTC,

探讨了数种场景下疗效相关指标、不良反应预防及治疗等内容, 报告了我国专家学者在 DTC 管理中做出的不懈努力。期待本期重点号能为<sup>131</sup>I 治疗的个体化管理提供思路, 为我国甲状腺癌相关领域的医师与工作人员带来启发。

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