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甲状腺癌的过度诊疗与精准规避策略

——基于循证医学与风险分层模型的整合分析

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摘　要

背景：甲状腺癌尤其是乳头状甲状腺癌(Papillary Thyroid Carcinoma, PTC)全球发病率在过去30年间显著激增。根据GLOBOCAN 2022数据，2022年全球新发甲状腺癌病例约82.12万例，年龄标准化发病率(ASIR)持续上升，但同期死亡率保持相对稳定(约4.75万例，年龄标准化死亡率约0.5/10万)，这一“流行病学悖论”强烈提示过度诊断(overdiagnosis)和过度治疗(overtreatment)已成为重大公共卫生问题。大量检出的微小癌(直径 ≤ 1 cm的甲状腺微小乳头状癌，PTMC)多为惰性肿瘤，一生中不会引起临床症状或威胁生命，却因传统“诊断即手术”模式导致不必要的手术、放射性碘治疗及终身激素替代，带来手术并发症(如喉返神经损伤、甲状旁腺功能减退)、心理负担、就业歧视和巨额医疗支出。近年来，中国作为发病率增长最快的国家之一，这一问题尤为突出，城市地区PTMC检出率已超过50%。目的：本综述系统分析甲状腺癌过度诊疗的驱动因素，评价现行规避策略(如主动监测)的有效性、安全性与局限性，并探讨分子标志物、影像组学及人工智能等新型工具在风险分层中的应用价值，最终提出整合多维度参数(临床－病理－分子－影像－患者偏好)的精准决策路径，以实现从经验驱动向数据驱动的转变。结论：甲状腺癌过度诊疗是多因素驱动的系统性问题。通过多层次风险分层，可有效区分惰性肿瘤与真正高风险病例，推动诊疗模式从“一刀切”向“个体化、精准化”转变。未来需加强本土化证据积累、完善医保政策、优化多学科协作(MDT)并提升医患共同决策能力，以实现患者获益最大化和医疗资源合理分配。

关键词

甲状腺微小乳头状癌，过度诊疗，主动监测，精准诊疗

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Overdiagnosis and Overtreatment of Thyroid Cancer and Precision Mitigation Strategies

—An Integrated Analysis Based on Evidence-Based Medicine and Risk Stratification Models

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Abstract

Background: The global incidence of thyroid cancer, particularly papillary thyroid carcinoma (PTC), has risen markedly over the past three decades. According to GLOBOCAN 2022 data, there were approximately 821,200 new cases of thyroid cancer worldwide in 2022, with a persistent increase in the age-standardized incidence rate (ASIR). In contrast, the mortality rate remained relatively stable during the same period (about 47,500 deaths, with an age-standardized mortality rate of approximately 0.5 per 100,000 population). This "epidemiological paradox" strongly indicates that overdiagnosis and overtreatment have emerged as critical public health problems. The vast majority of detected microcarcinomas, namely papillary thyroid microcarcinoma (PTMC, defined as tumors with a diameter ≤ 1 cm), are indolent neoplasms that do not cause clinical symptoms or threaten life throughout a patient's lifetime. However, the traditional "diagnosis-equals-surgery" model has led to unnecessary surgeries, radioactive iodine therapy and lifelong hormone replacement, resulting in surgical complications (e.g., recurrent laryngeal nerve injury, hypoparathyroidism), psychological distress, employment discrimination and substantial medical expenses. In recent years, as one of the countries with the fastest-growing thyroid cancer incidence, China has been confronted with an especially severe situation: the detection rate of PTMC in urban regions has exceeded 50%. Objective: This review systematically analyzes the driving factors underlying the overdiagnosis and overtreatment of thyroid cancer, evaluates the efficacy, safety and limitations of current mitigation strategies (e.g., active surveillance), and explores the application value of novel tools including molecular markers, radiomics and artificial intelligence in risk stratification. Ultimately, it proposes a precise decision-making pathway integrating multi-dimensional parameters (clinical, pathological, molecular, imaging and patient preferences), aiming to realize the transformation from experience-driven to data-driven clinical practice. Conclusion: Overdiagnosis and overtreatment of thyroid cancer are systemic issues driven by multiple factors. Multi-level risk stratification can effectively distinguish indolent tumors from genuinely high-risk cases, facilitating the shift of the diagnosis and treatment paradigm from a "one-size-fits-all" model to individualized and precise management. Future efforts are required to strengthen the accumulation of localized evidence, improve medical insurance policies, optimize multidisciplinary team (MDT) collaboration and enhance the capability of physician-patient shared decision-making, so as to maximize patient benefits and achieve the rational allocation of medical resources.

Keywords

Papillary Thyroid Microcarcinoma (PTMC), Overdiagnosis and Overtreatment, Active Surveillance (AS), Precision Diagnosis and Treatment

1. 引言：问题的提出与重要性

1.1. 流行病学悖论：甲状腺癌发病率显著上升，但死亡率保持稳定

自 20 世纪 90 年代以来，甲状腺癌尤其是 PTC 的全球发病率呈现爆炸式增长[1] [2]。根据 GLOBOCAN 2022 数据，2022 年全球新发甲状腺癌 82.12 万例[3]，较 1990 年增长超过 5 倍，美国、韩国、中国、意大利等国家发病率增幅尤为显著[4]-[6]。韩国曾在 2000~2010 年间发病率一度位居全球首位(女性年龄标准化发病率高达 90/10 万以上)，但在停止大规模筛查后发病率迅速回落近 70%，有力证明了筛查驱动的过度诊断[7]-[10]。中国情况类似：1990~2021 年间，年龄标准化发病率从约 1.2/10 万上升至 2.5/10 万以上，城市地区增长更快，2021 年新发病例约 4.8 万例，且 PTMC 占比超过 70% [11]-[14]。

然而，与发病率激增形成鲜明对比的是，甲状腺癌死亡率长期保持稳定甚至略有下降，2022 年全球死亡约 4.75 万例，年龄标准化死亡率仅 0.5/10 万[15] [16]。这一悖论的核心在于“过度诊断”：大量通过高分辨率影像学检出的微小、惰性肿瘤被诊断为“癌”，但这些肿瘤在自然病程中极少进展或致死[16] [17]。尸检研究显示，隐匿性甲状腺癌在普通人群中的检出率可达 4%~36%，远高于临床诊断率，充分印证了影像学筛查驱动的过度诊断现象[10] [18]。此外，早发型甲状腺癌(<40 岁)占比也在上升，2022 年全球约占 15.7%，其中近 99%可能为过度诊断[19]。

1.2. 过度诊疗的定义与范畴

过度诊断指诊断出那些在患者余寿中不会引起症状、并发症或死亡的肿瘤；过度治疗则指对这些惰性肿瘤实施不必要的侵入性干预[20] [21]。甲状腺癌领域，过度诊疗主要表现为：对低风险 PTMC 进行全甲状腺切除 + 中央区淋巴结清扫 + 放射性碘治疗，导致声带麻痹(发生率 1%~5%)、永久性甲状旁腺功能减退(1%~10%)、终身左旋甲状腺素替代及相关心血管风险、生活质量下降[22]。同时，患者面临“癌症”标签带来的心理创伤、焦虑抑郁(发生率高于普通人群 30%~50%)、就业歧视及高额医疗费用[10] [12]。全球范围内，过度诊疗每年造成数百亿美元经济负担，并占用宝贵医疗资源[19] [21]。在中国，患者自付比例较高，进一步加剧家庭经济压力和区域不公平。

1.3. 综述目的与路径

甲状腺癌过度诊疗是全球肿瘤诊疗领域的突出难题，既加重患者身心负担，又造成医疗资源浪费[1]。为破解这一痛点、为临床精准规范诊疗提供参考，本综述围绕“驱动因素分析 → 现行策略评价 → 精准工具探索 → 挑战与争议 → 实施路径 → 总结与展望”逻辑展开梳理：系统厘清过度诊疗多维度驱动机制，评估主动监测等现行规避策略的循证证据、安全性与成本效益，探索分子标志物、影像组学及 AI 在精准风险分层中的作用，剖析临床实施中的核心挑战与争议，最终构建适配中国国情的过度诊疗精准规避整合决策框架。下文将按此脉络逐章探讨，为临床实践、多学科协作和政策制定提供理论支撑与

决策依据。

2. 过度诊疗的现状与驱动因素：多层面分析

2.1. 技术驱动：影像技术的广泛应用与筛查普及

高分辨率超声、CT、MRI 等影像技术的进步是过度诊断首要驱动因素[23]。超声可检出直径仅 2~3 mm 的结节[24]，体检筛查普及后，PTMC 检出率急剧上升。美国 SEER 数据库显示，1990~2019 年间，直径 ＜2 cm 的甲状腺癌占比从 30%上升至 60%以上[25]。韩国“甲状腺癌风波”最具代表性：2000 年后超声筛查普及，发病率飙升 15 倍，但停止大规模筛查后发病率迅速回落，证实多数新增病例为过度诊断[2] [23]。在中国，商业化体检中心超声筛查普及是主因，城市女性检出率尤高，进一步放大问题[26]。

2.2. 病理学驱动：FNA 普及与诊断局限性

细针穿刺活检(FNA)结合 Bethesda 系统显著提高了诊断准确性，但对“不确定意义非典型病变”(AUS/FLUS, Bethesda III/IV 类)结节的恶性风险评估仍存在灰区(15%~50%)，分子检测虽可辅助但普及率低[27] [28]。同时，对“癌”的病理诊断标准相对宽松(如乳头状核特征即可诊断 PTC)，加之医患对“癌”字的恐惧，常引发治疗冲动[29]-[31]。即使是低风险 PTMC，传统模式仍倾向手术[32]。2016 年 NIFTP 再分类减少了 20%~30%“癌”诊断，但既往过度诊疗影响已成事实[33]。

2.3. 临床实践驱动：传统模式惯性与决策偏差

长期以来，“诊断即手术”是甲状腺癌管理的主导范式[23]。医生担心漏诊进展风险、医疗纠纷，患者倾向“根治”以求安心[34]。此外，对主动监测长期依从性的担忧(如失访、心理负担)也阻碍保守策略推广[35] [36]。调查显示，美国仅有 30%~40%医师常规推荐 AS，中国基层医师接受度更低[37]。

2.4. 社会文化驱动：公众心理与医疗环境

“谈癌色变”的社会心理、对“零风险”的过度追求，以及部分地区商业化体检推动筛查，都是重要驱动因素[38] [39]。中国等发展中国家发病率仍在上升阶段，公众筛查热情高涨，进一步放大过度诊疗问题[40]。同时，医保政策对“观察”支持不足，导致患者倾向手术以获得报销[41]。

2.5. 驱动因素的协同耦合关系

本文将过度诊断的驱动因素归纳为技术、病理、临床、社会四大维度，该分类框架能够系统覆盖核心影响要素，但需明确的是：四类因素并非独立发挥作用，而是形成相互嵌套、协同放大的耦合效应。单一因素仅为过度诊断提供潜在可能，而多因素间的交互作用才是推动过度诊断形成规模化、趋势化浪潮的核心动力。技术进步为筛查提供硬件基础，社会场景拓展为技术应用提供落地场景，临床诊疗规范与病理认知偏差进一步放大诊断阈值宽松化效应，最终形成“技术赋能－场景普及－临床落地－社会强化”的正反馈循环，共同加剧过度诊断风险。

3. 现行核心规避策略：主动监测 vs.手术干预

3.1. 主动监测：理念与实施

主动监测(Active Surveillance, AS)是对低风险 PTMC 不立即手术，而是定期影像学随访、出现进展征象时再干预的策略[1]。其理念源于肿瘤惰性自然病程，大量证据显示 PTMC 年进展率仅 2%~10% [16]。

循证基石：日本 Kuma 医院率先开展的前瞻性研究最具说服力，2025 年长期随访(中位 15~30 年)显示，肿瘤增大≥3 mm 比例仅 8%~10%，淋巴结转移约 3%，无癌特异性死亡[23]。美国 MSKCC、韩国多

中心研究及2024~2025年meta分析进一步证实，AS与立即手术在肿瘤特异性生存率(接近100%)和总生存率上无显著差异，尤其老年患者获益更大(手术并发症风险降低70%以上，生活质量更高) [42]。2025年巴西研究显示，AS长期成本显著低于手术[43]。

适应症标准：2025 ATA指南首次将AS作为低风险PTMC (直径 ≤1 cm、无侵袭证据、位置安全)首选管理策略[23] [44] [45]。日本2024修订指南最保守，韩国2025 KTA指南明确AS适应症并限制筛查[2] [46]。中国CACA 2022指南首次将AS列为可选方案，2025年解读进一步强化个体化，推荐年龄 > 60岁、合并症多者优先AS [47]。

监测方案：通常每6个月超声 + 甲状腺功能检查，前2年密集，后每年1次。进展定义：直径增大≥3 mm、新发可疑淋巴结或出现侵袭征象，此时转为手术[2] [48]。患者生活质量研究显示，AS组焦虑初期略高，但长期与手术组相当，甚至更好[1] [48] [49]。

3.2. 手术干预的降级策略

对需手术病例，策略已显著“去激进化”。腺叶切除取代全切除成为低风险PTC主流(2025 ATA推荐)，保留对侧腺体减少终身激素替代需求[44] [45] [50]。中央区淋巴结清扫从预防性转为选择性，仅限于临床阳性或高风险特征者[51]。术后TSH抑制目标根据风险分层调整，低风险者可放宽至正常范围上限，减少心血管副作用[51]。

3.3. 策略选择的困境

尽管证据充分，AS接受度仍较低。患者心理负担(“带着癌生活”)、医患决策冲突、区域医疗资源不均衡(如基层随访能力不足)是主要障碍。成本分析显示，AS可节省30%~50%医疗费用，尤其适合老年和低收入患者[46]。

4. 迈向精准规避：新型分层工具与整合应用

4.1. 分子标志物驱动分层

BRAF V600E突变(PTC中最常见，发生率40%~80%)与侵袭性相关，但单独预测价值有限[52] [53]。TERT启动子突变(发生率10%~20%)与不良预后高度相关，尤其是BRAF + TERT“双阳性”时，复发和死亡风险显著增加[54] [55]。2025~2026年多项研究证实，在PTMC中，双阴性者进展风险 < 5%，适合AS [56]；双阳性者建议积极干预。此外，基因表达分类器(如Afirma GSC)在Bethesda III/IV结节中阴性预测值 > 95%，可避免30%~50%不必要诊断性手术[57]-[59]。

尽管上述分子标志物与基因检测工具为甲状腺肿瘤精准分层提供了坚实的理论与循证依据，但其在真实世界临床中的落地应用仍存在显著结构性障碍，尤其在发展中国家，此类障碍已从根本上制约了精准分层策略的规模化推行，仅用“普及率较低”远不足以揭示问题的核心[60]。其一，检测成本居高不下，BRAF、TERT靶点检测及基因表达分类检测均依赖专用试剂与检测平台，多数发展中国家尚未将其纳入医保报销范畴，高额自费成本使其难以成为基层临床常规检查项目，直接阻断了精准分层在中低收入人群中的普及；其二，技术可及性存在显著区域不均，分子检测平台与专业检测人员多集中于大型中心城市医院，基层医疗机构、偏远地区缺乏配套设备与标准化实验室，样本转运周期长、检测渠道匮乏，进一步限制了分子标志物的临床可及性；其三，全流程标准化质控体系缺失，不同机构在样本处理、实验操作、结果判读等环节缺乏统一规范，检测结果的准确性与可比性难以保障，临床医师对检测结果的信任度不足，无法放心依据分子分层制定诊疗决策[61] [62]。上述多重障碍并非单纯的推广滞后问题，而是从经济可行性、资源覆盖性与结果可靠性三个维度，共同限制了分子标志物指导下的精准分层策略在发

展中国家真正发挥规避过度诊断、优化诊疗决策的核心价值[62]。

4.2. 影像组学与人工智能

超声影像组学提取数百个定量特征，结合 AI 模型(如 TI-RADS 优化版)可显著提高恶性风险预测准确性(敏感性 ＞90%)，并可预测淋巴结转移和包膜外侵犯[24] [63]。2024~2025 年研究显示，AI 辅助下误诊率下降 20%~30% [64]。未来动态影像组学有望用于 AS 中进展监测，结合 ctDNA 液体活检实现无创动态评估[44] [65]。

4.3. 临床－病理－分子整合风险模型

传统模型如 ATA 风险分层、MACIS 评分已较为成熟，但分子整合模型更精准[66]。韩国 2025 K-RSS 将 BRAF 状态纳入，将 1~2 cm BRAF 阳性 PTC 降为较低风险[9] [67]。未来方向是构建动态模型，整合临床(年龄、性别)、影像(组学特征)、分子(多基因面板)和真实世界数据，实现个性化风险概率量化[68] [69]。

5. 实施挑战与争议

5.1. 证据局限性

AS 最长随访数据约 30 年，但>20 年超长期数据仍不足[70] [71]。分子检测在真实世界中的成本－效益比需更多验证，尤其发展中国家[72]。

5.2. 病理再分类的冲击

2016 年 NIFTP (非浸润性滤泡性甲状腺肿瘤伴乳头状核特征)再分类将部分既往“癌”降为“非恶性”，全球范围内减少了约 20%~30% PTC 诊断，进一步证实过度诊断并影响既往发病率统计[73] [74]。

5.3. 医疗系统与支付障碍

AS 需要长期规范随访，基层医疗机构能力不足[75] [76]。医保政策多不覆盖“观察”费用，患者自付负担重。中国需探索将 AS 纳入医保或专项基金[77] [78]。

5.4. 医患沟通与共同决策

有效沟通“不确定性”是关键。需建立标准化决策辅助工具(如风险计算器、患者决策板)，帮助患者理解 AS 安全性，实现真正共同决策。研究显示，良好沟通可提高 AS 接受率 50%以上[79]-[81]。

6. 总结与展望：未来精准诊疗生态的构建

6.1. 核心结论

甲状腺癌过度诊疗根源于影像学过度筛查与传统激进模式。通过主动监测、分子分层及影像 AI 整合，可精准区分惰性与高风险肿瘤，显著减少不必要干预，改善患者预后和生活质量。

6.2. 临床实践建议

提出风险为基础的决策路径图：① 高危人群(家族史、辐射暴露)限度筛查；② 可疑结节优先高分辨超声 + TI-RADS 评估；③ FNA 不确定结节先分子检测(如 Afirma)；④ 确诊低风险 PTMC 首选 AS (尤其老年)；⑤ 分子/影像高风险者个体化手术(腺叶切除为主)；⑥ 全程 MDT 讨论 + 医患共同决策；⑦ 长期随访数据上报全国注册系统。

6.3. 未来研究方向

① 开发中国人群特异性整合风险模型(纳入遗传、环境因素)；② 探索 ctDNA 液体活检在 AS 动态监测中的价值；③ 利用真实世界大数据建立诊疗质量评估体系，持续抑制过度诊疗；④ 加强公众教育，遏制商业化筛查；⑤ 完善医保政策，支持 AS 和分子检测。最终构建“筛查规范–诊断精准–治疗个体化–随访智能化”的甲状腺癌诊疗新生态，实现公共卫生效益最大化。

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