·菁英论坛·

消化道癌前状态及癌前病变的内镜下随访策略

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【提要】 消化道肿瘤在全球癌症相关发病率和死亡率的比例居高不下。大多数上消化道肿瘤是由癌前疾病发展而来，包括慢性萎缩性胃炎、肠上皮化生和不典型增生，而下消化道肿瘤多起源于高风险结直肠息肉。消化内镜筛查是早期诊断上述消化道肿瘤高风险患者、预防消化道癌症相关死亡的关键策略。众多指南建议消化道肿瘤高风险患者应定期按时复查消化内镜，可大大提高早期诊断和治疗率。本文对消化道癌前状态及癌前病变的内镜下随访策略进行全面系统的综述，为临床随访工作提供循证医学依据，也为后续消化道随访领域的相关研究奠定理论基础。

【关键词】 消化道肿瘤；　癌前状态；　癌前病变；　内镜；　随访

Endoscopic surveillance for precancerous conditions and lesions in the digestive tract

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一、背景

消化道肿瘤占所有癌症发病率的 1/4 和死亡率的 1/3，是全球重大公共卫生问题[1]。消化道肿瘤包括食管癌（esophageal cancer，EC）、胃癌（gastric cancer，GC）和结直肠癌（colorectal cancer，CRC）等。食管癌是我国第五大癌症相关死亡原因，每年死亡病例超 187 500 例[2-5]。胃癌是我国第五大常见恶性肿瘤和第三大癌症相关死亡原因，每年新发病例超过 358 700 例，死亡病例超 260 400 例[3,5-8]。结直肠癌在我国为第二大常见恶性肿瘤和第四大癌症相关死亡原因，每年新发病例超 517 100 例，并导致了约 240 000 例患者死亡[5,9-11]。

早期诊断可显著改善消化道肿瘤患者的预后，但消化道肿瘤患者在早期阶段往往缺乏典型的临床表现，或仅表现出非特异性症状，通常直到晚期才可能出现临床症状[12-14]。因此，60%~80% 的消化道肿瘤患者在确诊时已处于中晚期[15]，五年存活率不足 20%，而早期患者的五年生存率可达 95%[16-19]。胃肠道肿瘤的早诊早治可减少约 1/3 的癌症相关死亡率，是提高患者生存率的关键策略[19]。消化内镜作为消化道肿瘤最直观有效且经济效益高的筛查手段[20-23]，可通过早期诊断及切除消化道肿瘤和癌前状态或癌前病变，降低消化道癌症相关发病率和死亡率[24]。

各国指南均建议消化道癌前状态及癌前病变患者因患癌风险高，应定期按时复查消化内镜，以提高早期诊断和治疗率[25-28]。合理的随访间隔至关重要，延迟随访错过最佳干预时机，导致患者的肿瘤发病率和死亡率显著增加[29-31]；同时，过于频繁或过早的随访则会增加患者的经济负担和医疗系统的压力，降低了随访的成本效益[20,32-33]。因此，对消化道癌前状态及癌前病变患者进行系统性的随访和科学管理已成为消化道肿瘤防治工作的重要内容。然而，由于临床医师对于不同指南的理解可能不同，不同医师向患者推荐的随访建议具有明显异质性[34-36]。因此，本文系统综述国内外食管、胃、结直肠癌前状态及癌前病变的内镜下随访策略及未来发展方向，为临床随访工作提供循证医学依据，也为后续消化道随访领域的相关研究奠定理论基础。

二、食管癌前状态和癌前病变的内镜下随访策略

（一）食管癌前状态和癌前病变的定义及发病情况

根据组织学分型，食管癌主要包括食管腺癌（esophageal adenocarcinoma，EAC）和食管鳞状细胞癌（esophageal squamous cell carcinoma，ESCC）[37]。流行病学数据显示两者存在显著的地域差异，ESCC 占全球食管癌的

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90%~95%[38-39]，高发区集中于东亚、中南亚以及南非，而EAC在欧美国家更为常见。中国的EAC和ESCC病例在全球占比分别为18%和53%，而我国90%的食管癌为ESCC[38-41]。

根据美国胃肠病学会（American College of Gastroenterology，ACG）的定义，巴雷特食管（Barrett Esophagus，BE）是指远端食管鳞状上皮发生肠上皮化生（intestinal metaplasia，IM）的一种病理状态，已被确认为EAC的癌前状态[42]。其典型的进展模式为糜烂性食管炎→BE→低级别异型增生（low-grade dysplasia，LGD）→高级别异型增生（high-grade dysplasia，HGD）→EAC[43]。BE在成人中患病率约2%，其中每年有0.5%~1%的患者进展为EAC[44-45]。

既往认为贲门失弛缓症、食管腐蚀性损伤、食管白斑、食管乳头状瘤等疾病可能增加ESCC风险，但由于这些疾病临床罕见，如食管乳头状瘤检出率仅0.01%~0.45%[25,46]，其人群筛查价值有限。

食管异型增生与食管癌的发生密切相关，食管黏膜经历轻度、中度、重度异型增生等癌前病变阶段，最终发展为原位癌[47-48]。2010年世界卫生组织（World Health Organization，WHO）引入了“上皮内瘤变”，用于描述异型增生和原位癌（carcinoma in situ，CIS）。根据该分类，低级别上皮内瘤变（low grade intraepithelial neoplasia，LGIN）包括轻度和中度异型增生，高级别上皮内瘤变（high grade intraepithelial neoplasia，HGIN）包括了重度异型增生和原位癌[41,49]。大规模人群研究表明，无异型增生者食管癌年进展率不足0.3%[50-52]，而LGIN和HGIN的进展风险分别达35%和75%[53]。

鉴于ESCC癌前状态相关疾病的极低发病率，且HGIN生物学行为与早期食管癌近似，通常将其归类为早期食管癌，本综述将聚焦更为常见的BE和LGIN的随访策略。

（二）食管癌前状态和癌前病变的内镜下监测与随访

1.BE的内镜下监测与随访：ACG 2022年指南推荐BE患者应定期行白光内镜和染色内镜检查，并使用西雅图活检方案（Seattle protocol），以最大程度减少BE的检测偏倚[54]。ACG建议无异型增生的BE患者，<3 cm者每5年复查，≥3 cm者每3年复查[54]；而美国胃肠病协会（American Gastroenterological Association，AGA）2022年建议非异型增生的BE患者应3~5年内接受内镜随访[55]。对于伴有LGIN的BE患者，ACG建议确诊后6、12个月各复查一次，此后每年复查[54]。

欧洲胃肠内镜学会（European Society of Gastrointestinal Endoscopy，ESGE）2023年指南则进一步细化BE长度分层：1~<3 cm者每5年监测，3~<10 cm者每3年监测，≥10 cm者应转诊至专门研究BE的医院进行监测，以便获得更专业的诊断和治疗[56]。中国共识提出独特建议：对<3 cm且不伴有IM或异型增生的BE，若二次内镜四象限活检后确认无IM，可中止随访；伴有IM者建议3~5年复查，≥3 cm者缩短至2~3年复查[28]。日本目前尚未建立BE的统一监测方案，但临床实践中多采用靶向活检而非西方常用的随机活检策略[57]。

2.食管LGIN的内镜下监测与随访：如前所述，ACG建议食管LGIN患者需在6和12个月各复查一次后转为年度随访[54]。中国共识则推荐更宽松的1~2年随访间隔，但强调需使用染色内镜配合靶向活检策略[25]。

三、胃癌前状态和癌前病变的内镜下随访策略

（一）胃癌前状态和癌前病变的定义及发病情况

根据Lauren分型，胃癌可分为肠型、弥漫型及混合型，其中，胃腺癌是最常见的组织学类型。胃癌的发生遵循Correa级联反应模式：从非活动性或慢性活动性胃炎，逐步经历慢性萎缩性胃炎（chronic atrophic gastritis，CAG）、IM以及异型增生（上皮内瘤变），最终发展为胃癌[58-59]。CAG与IM被认为是胃癌常见的癌前状态，上皮内瘤变则是胃癌前病变，三者可将胃癌的发生风险增加10倍以上[60-62]。

胃癌筛查数据显示，CAG的患病率为25.8%，IM为23.60%，上皮内瘤变为7.30%，且均呈逐年增加的趋势[63]。西方人群中每年约有0.1%的CAG患者、0.25%的IM患者、0.6%的LGIN患者和6%的HGIN患者进展为胃癌[64]。相比之下，东亚人群年进展率更高，每年约有1.8%的CAG患者、10%的IM患者以及73%的异型增生患者进展为胃癌[65]。其中不完全性和广泛性IM患者的癌变风险分别是完全性和局限性IM患者的3.3倍和2.1倍[66-68]。鉴于管理癌前状态和癌前病变是胃癌预防与控制中的关键步骤，本综述将重点探讨CAG、IM和LGIN的内镜随访策略。

（二）胃癌前状态和癌前病变的内镜下监测与随访

1.CAG内镜下监测与随访：AGA（2021年）和ESGE（2019年）均建议重度CAG患者每3年随访一次，但轻中度萎缩患者的随访证据不足[69-70]。英国胃肠病学会（British Society of Gastroenterology，BSG）推荐广泛性CAG每3年随访，局限于胃窦的CAG患者仅存在胃癌家族史或持续的幽门螺杆菌感染等风险因素时每3年随访[71]。日本同样提出轻度CAG目前不需要监测，而中重度CAG更可能从监测计划中获益，并应根据患者相对癌症风险确定监测频率[72]。2020年中国共识建议重度CAG每1~2年随访，轻中度CAG每3年行一次胃镜检查[26]。2022年中国指南建议广泛性CAG患者每年随访，局限性CAG每3年随访，有胃癌家族史者1~2年随访一次[59]。

2.IM内镜下监测与随访：2020年AGA指南不建议对IM患者常规监测，仅对胃癌高风险的IM患者（如不完全性IM、广泛性IM、有胃癌家族史等）建议1年内复查[73]。ESGE于2019建议对局限性IM伴胃癌家族史或不完全性IM者3年随访[70]。BSG指南建议广泛性IM每3年随访，局限性IM患者仅在高风险因素（如胃癌家族史或持续幽门螺杆菌感染等）存在时每3年进行一次监测[71]。日本指南推荐IM患者1~3年监测，而韩国国家癌症筛查计划（National Cancer Screening Program，NCSP）对40岁以上人群统一实施2年筛查[74]。中国指南建议广泛IM每年随访，尤其是有胃癌家族史者[59]，另有共识则根据胃黏膜萎缩的严重程度，推荐伴

IM的轻中度CAG患者每2~3年随访[26]。

3. 胃LGIN内镜下监测与随访：对于内镜下可见的LGIN，ESGE（2019年）、BSG（2019年）和中国指南（2022年）均建议立即治疗[59,70-71]。对于非可见LGIN，ESGE推荐每年复查[70]；BSG则要求在增强成像下二次检查并进行广泛活检，若仍不可见则每年随访[71]；中国指南建议通过高清染色内镜重新评估，若仍没有发现可见LGIN，则6~12个月复查高清染色内镜[59]。中国共识于2020年提出，对于高清染色内镜检查显示边界不清和边界清晰的LGIN患者，分别推荐每年或每6个月进行一次高清染色内镜复查[26]。

四、结直肠癌前状态和癌前病变的内镜下随访策略

（一）结直肠癌前状态和癌前病变的定义及发病情况

结直肠癌的发生发展主要涉及两条关键途径：传统的腺瘤—癌序列途径（占60%~90%病例）和锯齿状途径[75-81]。在常规的腺瘤—癌序列途径中，通常表现为正常上皮经管状或绒毛状腺瘤逐渐癌变的过程[81-82]。因此，管状、管状绒毛状或绒毛状腺瘤为代表性癌前病变[81-82]。结直肠锯齿状息肉在组织病理学上分为增生性息肉（hyperplastic polyps，HPs）、无蒂锯齿状病变（sessile serrated lesions，SSL）和传统锯齿状腺瘤（traditional serrated adenomas，TSA）。在锯齿状肿瘤途径中，HPs是最普遍的非恶性病变，SSL和TSA被视为癌前病变，在癌变过程中起着重要作用[83-86]。

流行病学数据显示，50岁以上人群腺瘤检出率达20%~53%，其中进展期腺瘤（即直径≥10 mm、具有绒毛状成分或伴有HGIN）占9.7%[87-88]，其结直肠癌发病率（13.81/万人年）显著高于无腺瘤患者（3.4/万人年）[89-90]。SSL平均患病率约2.7%，晚期肿瘤风险是非SSL患者的3.53倍[91-95]。TSA是最为罕见的锯齿状息肉，仅占1%~7%，但其结直肠癌累积发病率达1.34%，结直肠癌累积死亡率达0.12%，显著高于正常患者[96-102]。

慢性炎症是肿瘤进展的关键驱动因素，可在结肠多个区域形成癌前病变。炎症性肠病（inflammatory bowel disease，IBD）作为典型的慢性炎症性疾病，是结直肠癌主要的癌前状态之一[103-106]。IBD主要包括溃疡性结肠炎（ulcerative colitis，UC）和克罗恩病（Crohn disease，CD）两种主要类型，其发病率约10.04/10万人年，患病率达0.5%[107-111]。与非IBD人群相比，IBD患者罹患结直肠癌的风险显著增加2~3倍；且与散发性结直肠癌相比，IBD相关结直肠癌的总体生存率也较低[112-115]。

由于TSA的罕见性，本综述主要聚焦于结直肠腺瘤、SSL以及IBD的随访策略展开探讨。

（二）结直肠癌前状态和癌前病变的内镜下监测与随访

1. 结直肠腺瘤的内镜下监测与随访：对于低风险病变，2022年亚太共识建议1~2个<10 mm管状腺瘤患者5~10年后复查结肠镜和（或）粪便免疫化学试验（fecal immunochemical test，FIT）[116]，2022年中国共识则推荐1~3年间隔[27]，ESGE 2020年指南则认为1~4个<10 mm无HGIN腺瘤无需专门随访[117]。在高风险病变监测方面，中国共识建议每1~2年随访一次[27]，其他指南普遍将≥10 mm腺瘤、绒毛状腺瘤和（或）伴HGIN作为3年随访标准，但在腺瘤数量阈值的规定存在差异：亚太共识≥3个[116]；英国胃肠病学会/大不列颠及爱尔兰结肠直肠学会/英国公共卫生部（British Society of Gastroenterology/Association of Coloproctology of Great Britain and Ireland/Public Health England，BSG/ACPGBI/ PHE）2020年指南要求≥2个且至少含1个高风险特征，或≥5个腺瘤或锯齿状息肉[118]；韩国2022年要求5~10个[119]；ESGE≥5个[117]。韩国对3~4个腺瘤建议3~5年间隔[119]；中国共识则对3~10个腺瘤采取更密集的1~2年随访[27]。特殊情况下，韩国和ESGE指南均建议≥20 mm分块切除者6个月内复查，>10个腺瘤患者推荐1年间隔或遗传咨询[117,119]。日本消化内镜学会（Japanese Gastroenterological Endoscopy Society，JGES）目前对所有息肉切除患者推荐3年内随访，相当于欧美对高风险组的处理标准，未来需依靠长期随访数据进一步优化监测方案[120]。

2. SSL的内镜下监测与随访：亚太共识建议对>10 mm或伴异型增生的SSL每3年复查[116]。BSG/ACPGBI/PHE推荐<20 mm者3年复查，≥20 mm者2~6个月复查[118]。韩国指南要求伴异型增生、≥5个或≥10 mm者3年复查，3~4个者3~5年复查，≥20 mm分块切除者6个月复查[119]。ESGE建议≥10 mm或伴异型增生者3年复查，≥20 mm分块切除者3~6个月复查，<10 mm无异常者无需常规随访[117]。中国共识推荐<10 mm无瘤变者2~3年复查，>10 mm或伴瘤变者1~2年复查[27]。

3. IBD的内镜下监测与随访：ACG（2019年）和AGA（2021年）均建议IBD患者应在症状出现后8~10年开始监测，但随访间隔不同。ACG推荐IBD患者1~2年一次，原发性硬化性胆管炎（primary sclerosing cholangitis，PSC）患者每年一次[103]。AGA具体间隔根据风险分层确定：高风险患者（PSC、中重度炎症、一级亲属中有50岁以下的结直肠癌患者、密集假性息肉病、过去5年内有不可见的异型增生或高风险可见的异型增生史）每年一次；中风险患者（轻度炎症、有结直肠癌家族史但非50岁以下的一级亲属、既往有中度假性息肉或广泛黏膜瘢痕等严重结肠炎特征、5年前有不可见的异型增生或高风险可见的异型增生史、5年内有低风险可见的异型增生史）2~3年一次；低风险患者（自上次结肠镜检查后疾病持续缓解且当前检查显示黏膜愈合加上连续两次或以上检查无异型增生或既往结肠炎范围最小）5年一次[121]。

BSG（2019年）建议IBD患者在症状出现后8年开始监测[122]。高风险患者（广泛性结肠炎伴重度活动性炎症、过去5年内发现狭窄或异型增生、PSC、一级亲属中有50岁以下的结直肠癌患者）每年一次；中风险患者（广泛性结肠炎伴轻度至中度活动性炎症、假性息肉、一级亲属中有50岁以上的结直肠癌患者）3年一次；低风险患者（广泛性结肠炎且无活动性内镜或组织学炎症、左侧结肠炎、CD结肠炎累及范围小于50%的结肠）5年一次[122]。德国（2019年）的标

准与BSG基本相同，但中风险和低风险患者德国分别建议2~3年和4年复查一次[103]。

亚洲克罗恩病和结肠炎组织（Asian Organization for Crohn′s and Colitis，AOCC）和亚太地区胃肠病学协会（Asian Pacific Association of Gastroenterology，APAGE）和日本胃肠病学会（Japanese Society of Gastroenterology，JSG）于2020年均建议IBD患者应在症状出现后8年开始监测，但未明确分层或提供详细随访间隔[123-124]。JSG特别提出，平坦黏膜中发现LGIN的IBD患者需3~6个月复查结肠镜[103,124]。

中华医学会消化病学分会炎症性肠病学组（2020年）建议：UC患者应在诱导治疗的第3、4个月进行内镜复查；维持治疗的早期阶段于第6~12个月复查；长期维持且病情稳定时，每1~2年复查；病程超过8~10年或有多种肠外表现的癌变高风险，若广泛累及结肠，则应在确诊后8年开始1~2年监测一次，若为左半结肠炎的患者可在确诊后10年开始监测，如连续两次结肠镜检查未发现异常可延长至2~3年，若合并PSC，则应每年监测结肠镜；CD患者则需个体化随访，合并上消化道病变建议3~6个月复查胃镜，采用激素或免疫抑制剂治疗者1年后复查全结肠镜或小肠镜，采用生物制剂治疗者6~9个月后复查，并根据复查结果确定后续监测时间[125]。

五、研究展望

本文系统梳理了全球不同国家食管、胃及结直肠癌前状态和癌前病变的内镜随访策略，发现各地区基于各自流行病学特征制定了相应的临床随访指南。虽然这些指南为高风险患者的规范化管理提供了重要依据，但是目前超过50%的高风险患者未能在指南推荐的时间间隔内按时复查，且传统的依赖于人工进行的随访耗时耗力[126-129]。因此，未来随访相关领域研究应重点关注以下几个方面。

首先，各项临床指南的制定通常仅基于患者的镜下表现和病理特征，大多未结合患者个体化情况，如年龄、经济水平、并发症等。过于严格的监测可能并不适合所有患者，而对于具有较高疾病进展风险的患者群体，更需要重点关注。因此，在为患者制定随访策略时，应结合患者自身潜在的影响因素，进一步优化随访监测策略，提供个性化的随访方案。

其次，即使临床随访指南已明确高风险患者随访的必要性，在临床实践中医师在制定随访监测建议时也存在显著异质性，与临床随访指南的推荐也存在明显异质性，影响了患者随访管理的规范性和科学性[35-36]。人工智能（artificial intelligence，AI）技术的应用可能不仅能够优化随访过程，提高随访效率，还能够有效减少医师随访建议的个体差异，提高医师临床决策的准确性、客观性和一致性[130-131]。Wu等[131]将AI应用于结直肠息肉切除术后患者的随访管理，可自动识别需要随访患者的准确率达99%，并通过自动发送短信和拨打电话通知患者复查，实现高效随访。在前瞻性试验中，该AI系统自动随访患者的成功率达93.18%，与传统人工随访方式相比，AI随访显著减轻了医护人员的工作负担，将平均随访时间从2.86 h降至0 h[131]。

再次，临床随访策略的制定依赖于患者病灶的检出，病灶的高检出率和高准确率是随访策略合理准确的重要依据。未来可探索AI图像分析技术在提高癌前状态或癌前疾病检出率和准确率的应用潜能，以提升患者随访工作的有效性并改善患者预后结局。

最后，需要进一步开展全球多中心大规模前瞻性研究，以验证现有随访策略的有效性和安全性，并探索影响随访间隔分配的潜在因素，优化随访方案，促进全球高风险随访经验交流与学习，推动随访工作的统一性和科学性。

六、总结

消化道癌前状态及癌前病变是消化道肿瘤的重要危险因素，及时干预可显著降低消化道肿瘤的发病率和死亡率。因此，定期进行内镜检查可持续监测早期肿瘤的发生，提高早期诊断率和治疗率。本文系统总结了消化道（包括食管、胃和结直肠）癌前状态及癌前病变的定义、发病情况、进展风险以及各国家或地区的随访策略，旨在增强临床医师对高风险患者规律随访的意识，辅助制定合理随访计划，在减少医疗资源浪费的同时，减少消化道肿瘤的发生风险并改善患者预后。

利益冲突　所有作者声明不存在利益冲突

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