

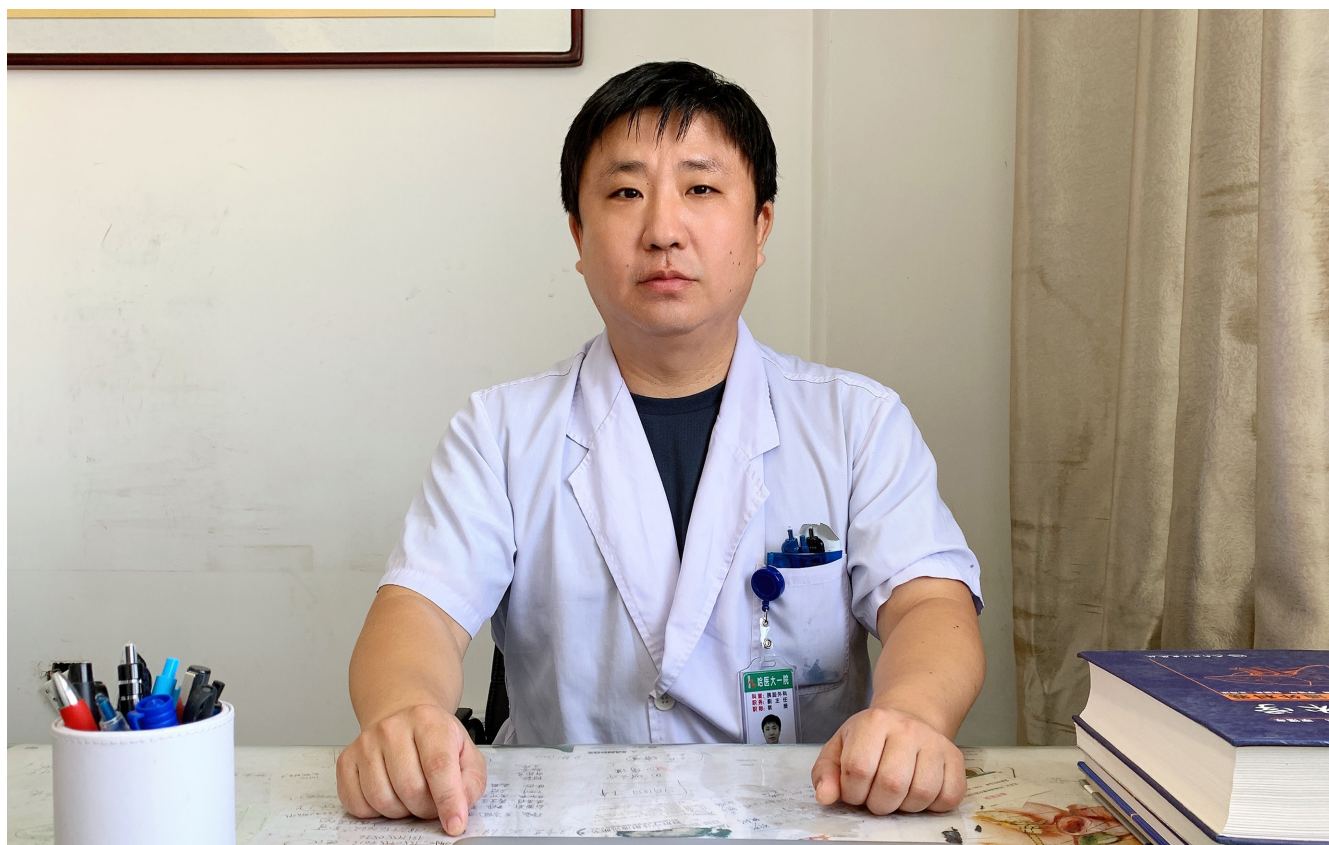
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结肠镜腺瘤检出率的近期研究进展

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Progress in understanding of factors related to colonoscopic adenoma detection rate

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Abstract

Adenoma detection rate (ADR) is the proportion of average-risk patients undergoing screening colonoscopy in whom an adenoma is found, and it is an important quality indicator of colonoscopy. ADR is closely related to the risk of interval colorectal cancer. A deeply study of ADR is essential for endoscopists. In this paper, we review the progress in the understanding of factors related to ADR before, during, and after colonoscopy, as well as several issues worthy of attention.

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Key Words: Adenoma detection rate; Colonoscopic; Colorectal cancer

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摘要

腺瘤检出率(adenoma detection rate, ADR)是指接受结肠镜筛查的一般风险人群中腺瘤检出的比例, ADR是结肠镜检查重要的质量指标. ADR与间期结直肠癌发生风险密切相关, 深入认识ADR对于内镜医师而言至关重要. 本文现就结肠镜检查前、结肠镜检查中与结肠镜检查后与ADR相关因素的研究进展, 以及值得关注的几个问题, 结合近年来国外文献进行了综述.

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关键词: 腺瘤检出率; 结肠镜; 结直肠癌

核心提要: 腺瘤检出率(adenoma detection rate, ADR)是结肠镜检查重要的质量指标。大样本研究结果表明ADR与间期结直肠癌(colorectal cancer, CRC)发生风险密切相关, ADR<20%的内镜医师其间期CRC发生率较ADR>20%者高10倍。ADR每增加1%, 间期CRC发生风险可降低3%, 致死性间期CRC降低5%。积极提高内镜医师自身的ADR有助于降低间期CRC及其相关死亡风险。

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0 引言

腺瘤检出率(adenoma detection rate, ADR)是指接受结肠镜筛查的一般风险人群中腺瘤检出的比例, ADR是结肠镜检查重要的质量指标^[1]。大样本研究结果表明ADR与间期结直肠癌(colorectal cancer: CRC; 即筛查未发现而在下一次筛查或监测之前发现的CRC)发生风险密切相关, ADR<20%的内镜医师其间期CRC发生率较ADR>20%者高10倍^[2]。ADR每增加1%, 间期CRC发生风险可降低3%, 致死性间期CRC降低5%^[3]。2015年美国胃肠病协会(American Gastroenterological Association, ACG)与美国胃肠内镜学会(American Society of Gastrointestinal Endoscopy, ASGE)联合工作组推荐行结肠镜筛查的≥50岁人群总体ADR≥25%, 其中男性≥30%、女性≥20%^[4]。积极提高内镜医师自身的ADR有助于降低间期CRC及其相关死亡风险^[5]。因此, 深入认识ADR对于内镜医师而言至关重要, 本文现就其近期研究进展加以综述如下。

1 结肠镜检查前与ADR相关的因素

1.1 肠道准备 分次剂量(检查前1 d+检查当天各服用1/2剂量)方案是目前推荐使用的结肠镜肠道准备方法^[4]。3项荟萃分析评估了分次剂量肠道准备对ADR的影响, 结果发现与检查前1 d肠道准备比较, 分次剂量的肠道清洁度明显更优^[6], ADR亦增加^[7], 与检查当天肠道准备比较, 两者肠道清洁度相似^[8], ADR也无统计学差异^[7,8]。加用消泡剂西甲硅油有助于进一步改善肠道准备质量, 特别是对于基线ADR低(<25%)的内镜医师更利于改善其ADR^[9]。

充分的肠道准备为内镜医师提供了良好的检查视野, ADR也明显优于不充分准备者^[4]。Guo等^[10]的研究在充分肠道准备基础上进一步提高其质量, 发现随波士顿肠道准备评分(boston bowel preparation scale, BBPS)增加, ADR亦随之增加(BBPS 6分, 21.8%; BBPS 7分,

27.8%; BBPS 8分, 28.2%; BBPS 9分, 32.6%), 肠段(右半结肠, 横结肠, 左半结肠) BBPS 3分者ADR最高。然而, Calderwood等^[11]的研究却发现随BBPS增加, ADR呈现下降趋势(BBPS 6分, 40.4%; BBPS 7分, 40.6%; BBPS 8分, 38.8%; BBPS 9分, 34.3%), 各肠段BBPS 2分者较3分的ADR高。随后Choi等^[12]的研究同样发现肠道准备良好(BBPS = 6, 7)组的ADR明显高于肠道准备优秀(BBPS = 8, 9)组, 认为进一步提高肠道准备质量对于ADR可能没有帮助。分析其原因, 考虑可能是优质的肠道准备易于麻痹分散内镜医师的注意力, 盲目地增加其自信心^[11], 而肠道粪便残渣和/或粘液的存在有助于突显息肉, 增加内镜医师的关注以及冲洗和吸引次数, 延长了内镜检查时间, 从而增加ADR^[12]; 其次, 应注意到的是, 肠道准备评分仍然存在一定的主观性, 相同的肠道条件下不同的内镜医师可能会分别给出2分或3分, 从而出现评分上的差异^[11,12]。

1.2 内镜时间安排 近期一项系统评价及荟萃分析评估了上午或下午结肠镜检查对ADR的影响, 总体分析显示结肠镜检查时间安排并不影响ADR, 但亚组分析发现内镜医师全天工作会导致下午的ADR明显降低^[13]。另一项荟萃分析亦发现上午或下午结肠镜检查的ADR无统计学差异, 但亚组分析并未发现内镜医师全天工作或仅半天工作对下午的ADR会产生明显影响^[14]。Lee等^[15]的一项基于社区的大样本研究也显示内镜医师疲劳不影响ADR。然而, 来自社区的研究结果并不一定完全适用于高强度的内镜中心工作^[16], 由于每个内镜医师的耐力各不相同, 有些内镜医师可能更容易受到疲劳的影响^[13]。因此, 内镜医师应注意保持清晰的意识, 积极监测自身疲劳, 从而避免影响结肠镜检查质量^[16]。

1.3 内镜医师特征与性格 一项来自美国克利夫兰医学中心的大样本回顾性研究, 在调整了已知与ADR相关的临床、患者和结肠镜检查变量之后, 通过多层次混合效应逻辑回归分析显示ADR与内镜医师的特征(专业、性别、就读的医学院所在地、培训结束后时间、每年结肠镜检查例数、所在医院以及结肠镜检查时存在学员)之间并无明显相关性, 认为上述特征并不影响腺瘤的检出^[17]。Ezaz等^[18]在统计美国多家医院117名内镜医师的ADR后对他们进行了问卷调查, 以评估ADR与内镜医师性格及经济之间的关系, 结果发现ADR与经济奖励、对医疗事故的担心、以及对ADR作为质量指标的了解之间无明显相关性, 但ADR与内镜医师自我报告更具强迫性或更细致明显相关。另一项来自韩国的多中心研究, 采用明尼苏达多相人格调查表(minnesota multiphasic personality inventory, MMPI-2)评估了20名内镜医师性格与ADR之间的关系, 结果发现两组内镜医师(ADR≥45% vs

<45% 各有10名)比较, MMPI-2临床评分(如疑病和精神病)、内容量表(如强迫性和A型性格)以及补充量表(如支配地位和社会责任)无明显差异, 在调整患者因素之后, 逻辑回归分析显示ADR与MMPI-2评估的自我力量显著相关, 认为自我力量强的内镜医师受各种环境因素的影响较小, 可以更细致的在退镜过程中去观察^[19]。目前有关内镜医师性格与ADR的相关资料尚少, 在结肠镜筛查过程中是否应考虑到这一因素, 还有待于进一步的研究证实。

2 结肠镜检查中与ADR相关的因素

2.1 镇静药物 镇静药物辅助的结肠镜检查对ADR的影响文献报道不一, 两项回顾性研究报道镇静药物辅助结肠镜检查较清醒状态明显提高患者的ADR, 多因素分析显示镇静药物辅助结肠镜检查与ADR独立相关^[20,21], 但另一项大样本的回顾性研究却显示使用镇静药物并不增加患者的ADR (13.0% vs 12.44%, $P = 0.337$)^[22]。近期一项纳入11项研究共计177016例患者的系统评价及荟萃分析, 比较了深度镇静(丙泊酚)与中度镇静(阿片类/苯二氮卓类药物)对ADR的影响, 结果发现丙泊酚并不优于阿片类/苯二氮卓类药物, 两者ADR相似, 建议临床应根据患者的风险, 个体化选择镇静药物^[23]。

2.2 插镜 盲肠插镜时间是结肠镜检查的能力指标^[1]。Hsieh等^[24]汇总4项有关盲肠插镜时间与ADR的研究, 结果发现盲肠插镜时间延长并未对ADR产生不利影响。水交换结肠镜检查是有别于常规注气的一种新的进镜技术, 一项纳入17项RCT的荟萃分析显示, 与水浸泡、注入空气、注入CO₂比较, 水交换检查方法尽管插镜时间有所延长, 但显著增加总体ADR以及右半结肠ADR, 并明显改善肠道清洁度^[25]。另一项荟萃分析在调整患者年龄、性别以及退镜时间之后, 同样发现水交换检查方法可以最大程度改善ADR^[26]。在插镜过程中是否需要仔细观察及息肉切除, 对此近期一项包括7项RCT的系统评价及荟萃分析显示, 与仅在退镜时仔细观察以及息肉切除比较, 在插镜时附加仔细观察及息肉切除尽管缩短了总体操作时间, 但并不改善ADR^[27]。

2.3 变换体位 结肠镜退镜过程中患者常位于左侧卧位或仰卧位, 适时变换体位有利于肠腔扩张, 从而更好的观察肠道黏膜^[4]。近期一项包括5项RCT的荟萃分析, 评估了退镜时动态变换体位(左侧卧位观察右半结肠, 仰卧位观察横结肠, 右侧卧位观察左半结肠)的效果, 结果显示与静态体位比较, 动态变换体位明显增加总体ADR, 特别是在横结肠段, 而退镜时间没有明显延长^[28]。另一项荟萃分析同样发现与静态左侧卧位比较, 退镜时动态

变换体位显著增加ADR, 退镜时间两组并无统计学差异 (12.43 min vs 11.46 min, $P = 0.27$), 提示根据所检查肠段的不同, 动态变换体位有利于腺瘤的检出^[29]。但是, 对于体重偏大者, 特别是镇静患者多次变换体位往往较为困难, 这也是其不足之处。

2.4 二次检查 目前常规结肠镜检查仍有可能漏诊结肠腺瘤, 特别是位于右半结肠的腺瘤^[1]。Kushnir等^[30]的一项多中心平行随机对照研究, 比较了结肠镜二次检查(第一次插镜到盲肠后退镜观察至肝曲, 然后再次插镜到盲肠第二次退镜观察)对右半结肠ADR的影响, 结果发现前视下二次退镜检查与倒镜下二次退镜检查的ADR相似, 两者与常规的一次退镜检查比较, 均可增加右半结肠ADR。Desai等^[31]系统评价了结肠镜二次检查, 结果发现与一次退镜检查比较, 前视或倒镜二次退镜检查均可明显提高右半结肠的ADR, 前视下二次退镜检查可增加10%的右半结肠ADR, 倒镜下二次退镜检查可增加6%的右半结肠ADR。考虑到有10%的内镜医师倒镜仍然会有所困难^[30], 前视下二次退镜检查简单方便, 值得内镜医师在结肠镜检查时常规应用。

2.5 内镜与染色 近期一项包括6项RCT共计4594例患者的荟萃分析显示高清白光结肠镜的ADR显著高于普通白光内镜 (40% vs 35%, $P = 0.001$)^[32]。染色亦有助于提高ADR^[33]。Kim等^[34]的一项多中心随机对照研究比较了退镜过程中喷洒靛胭脂对ADR的影响, 结果显示与常规结肠镜检查比较, 染色内镜明显改善ADR (54.4% vs 44.9%, $P < 0.001$), 但染色内镜的退镜时间亦长于常规内镜 (11.2 min vs 9.2 min, $P < 0.001$)。既往的研究显示应用窄带成像(NBI)、智能分光(FICE)或智能光学染色(i-scan)技术并不改善ADR^[33], 然而, 随着内镜设备以及电子染色技术的不断更新及应用, 近期Atkinson等^[35]纳入11项RCT进行荟萃分析, 结果发现总体而言NBI较高清白光明显增加ADR (45.2% vs 42.3%, $P = 0.04$), 在肠道准备优良时效果最好, 亚组分析显示二代NBI改善ADR, 而一代NBI则否。Shinozaki等^[36]的荟萃分析显示联动成像(LCI)较白光显著提高ADR。Kidambi等^[37]的一项大样本RCT研究同样发现i-scan较高清白光明显增加ADR (47.2% vs 37.7%, $P = 0.01$)。现今已有几种安装在结肠镜头端的黏膜暴露装置用于临床, 多项荟萃分析显示透明帽、EndoRings并不改善ADR^[26,33,38], 而Endocuff则有助于提高ADR^[26]。近年来, 基于深度学习的计算机辅助检查(computer-aided detection, CAdE)亦被应用于结肠镜检查当中, Hassan等^[39]纳入5项RCT共计4354例患者的荟萃分析显示, CAdE较对照组显著提高总体ADR (36.6% vs 25.2%, $P < 0.01$)。

2.6 退镜时间 退镜时间是指结肠镜自盲肠开始退镜直至退出肛门所花费的时间, 并除外切除息肉耗费的时间^[1]. 推荐的退镜时间应 ≥ 6 min^[4]. 一项来自韩国的前瞻性研究通过多因素分析发现, 右半结肠退镜时间 ≥ 2 min、近端结肠退镜时间 ≥ 4 min、左半结肠退镜时间 ≥ 3 min与ADR显著相关^[40]. 但另一项随机研究却显示与常规的自由退镜时间(≥ 6 min)比较, 固定的退镜时间(盲肠、升结肠 ≥ 2 min, 横结肠 ≥ 1 min, 左半结肠 ≥ 3 min)并未改善ADR (39.8% vs 42.1%, $P = 0.43$), 认为重要的是保持足够的退镜时间以利于仔细检查^[41]. 近期一项来自国内的多中心随机对照研究也证实, 进一步延长退镜时间至9 min较6 min显著增加ADR (36.6% vs 27.1%, $P = 0.001$)^[42].

3 结肠镜检查后与ADR相关的因素

3.1 反馈信息 一项研究对美国117名内镜医师进行了问卷调查, 发现大多数内镜医师(67.5%)并未接受到自身ADR信息的反馈, 而接受反馈的医师其ADR趋向高于未接受者(31.5% vs 28.4%, $P = 0.08$)^[18]. Bishay等^[43]的一项涉及154名内镜医师的荟萃分析, 评估了反馈结肠镜质量控制指标(ADR、盲肠插管率与退镜时间)对内镜医师的ADR影响, 结果发现总体ADR由反馈前的30.5%明显增加至反馈后的36.0%. Boregowda等^[44]涉及超过217名内镜医师的系统评价及荟萃分析, 同样发现与接受反馈之前比较, 主动或被动接受任何形式的质量反馈均可显著提高内镜医师的ADR (36.18% vs 26.75%, $P < 0.001$).

3.2 教育培训 内镜医师个体的ADR是间期CRC独立的预测因素^[2,3]. 研究表明通过培训可提高内镜医师的ADR, 降低间期CRC的发生风险^[5]. Lim等^[45]包括3项研究的系统评价及荟萃分析显示, 针对性的培训干预措施趋向于增加ADR. 另一项纳入8项研究的荟萃分析评估了教育干预对于ADR的影响, 结果发现总体ADR从教育之前的26.5%增加至教育干预之后的35.4%, 近端结肠ADR从之前的9.3%增加至教育干预之后的13.1%, 认为教育干预是提高结肠镜检查质量重要的改进措施^[46]. 近期美国ACG亦推荐ADR低于25%的内镜医师应接受继续教育^[1].

4 值得关注的几个问题

ADR是用于结肠镜筛查的质量指标^[4], 2017年欧洲胃肠内镜学会的质量改进计划指出ADR($\geq 25\%$)不仅仅局限于筛查结肠镜, 亦适用于所有的结肠镜检查^[47]. 两项来自美国的大样本研究发现, 监测结肠镜的ADR高于筛查结肠镜, 而筛查结肠镜的ADR又高于诊断性结肠镜, 总

体ADR (包括筛查、监测和诊断性结肠镜)与基于筛查结肠镜的ADR平均绝对差异仅为2.6%, 显示总体ADR同样可以有效地评估结肠镜质量, 并可增加用于检测ADR的患者例数^[48,49]. 2021年美国结直肠癌筛查指南亦指出, 当筛查结肠镜检查例数较少时, 可合并监测和诊断性结肠镜检查^[1]. 值得注意的是, 当前的ADR仅指常规腺瘤, 并不包括无蒂锯齿状病变(sessile serrated lesions, SSL), 后者与常规腺瘤属于不同的类别, 不计入ADR当中^[1,4]. 目前推荐的ADR $\geq 25\%$ 是指大于50岁的筛查人群^[4,47], 一项来自亚洲的大样本多中心研究评估了小于50岁(30-49岁)筛查人群的腺瘤检出情况, 结果发现ADR最佳的目标值与大于50岁的人群不同, 小于50岁筛查人群建议其ADR目标值 $\geq 20\%$ ^[50]. 尽管ADR有着诸多优点, 但也有其不足之处^[51,52]; (1)有可能导致“一劳永逸”的实践模式; 由于ADR与腺瘤数量无关, 使得内镜医师可能仅满足于发现1个腺瘤, 而忽略对其它可能存在的腺瘤进行检测; (2)ADR不能区分进展期或非进展期腺瘤, 而前者有更高的CRC发生风险, 且两者的随访监测策略也有所不同; (3)对于关注重点不是息肉检出的患者(如炎症性肠病), ADR价值有限; (4)ADR并不能反映内镜医师的腺瘤切除能力, 而完整的切除所检测到的腺瘤可能较腺瘤检出本身更为重要. 近年来, 有学者提出SSL检出率与进展期腺瘤检出率作为结肠镜质量指标, 但目前尚无这两者与间期CRC相关的文献报道, 仍需进一步的资料研究证实^[1].

5 结论

总之, 内镜医师的ADR与结肠镜检查术前、术中以及术后多种因素密切相关, 深入认识并积极改进对于提高内镜医师的ADR, 降低间期CRC发生风险十分重要. 然而, 目前尚不清楚ADR是否存在最大获益的上限值, 在此之上获益将不再增加, 对此仍然需要将来的研究进一步深入探讨.

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• 消息 •

《世界华人消化杂志》性质、刊登内容及目标

本刊讯 《世界华人消化杂志》[国际标准刊号ISSN 1009-3079 (print), ISSN 2219-2859 (online), DOI: 10.11569, *Shijie Huaren Xiaohua Zazhi/World Chinese Journal of Digestology*], 是一本由来自国内31个省、市、自治区、和香港特别行政区和719位胃肠病学和肝病学专家支持的开放存取的同行评议的半月刊杂志, 旨在推广国内各地的胃肠病学和肝病学领域临床实践和基础研究相结合的最具有临床意义的原创性及各类评论性的文章, 使其成为一种公众资源, 同时科学家、医生、患者和学生可以通过这样一个不受限制的平台来免费获取全文, 了解其领域的所有的关键的进展, 更重要的是这些进展会为本领域的医务工作者和研究者服务, 为他们的患者及基础研究提供进一步的帮助。

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