

内镜在食管癌中的治疗作用与评价

American Society of Gastrointestinal Endoscopy

编者按 该指南是消化内镜在常见临床情况下应用的系列讨论之一. 由美国消化内镜学会(ASGE)提供. 在撰写这一指南的过程中, 除MEDLINE检索到的相关文献外, 还参考了一些专家推荐的文章. 内镜的合理应用指南基于目前的一些重要的综述和专家共识. 还需要大量临床对照研究加以确定和必要的修订. 当临床实际情况与指南有所差异时影视当调整应适当调整.

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0 引言

在美国, 每年大约有 13 000 个患者被诊断为食管癌^[1], 并且食管腺癌是恶性肿瘤中发生率升高最快的^[2]. 食管癌可在内镜普查高风险疾病如 Barrett's 食管时被发现^[3], 而大部分新近诊断为食管癌的患者都有一定的症状, 并未经过普查^[4]. 该指南旨在为食管癌的内镜诊断、分期和治疗提供最新、实用的原则.

1 诊断

1.1 内镜诊断 标准上消化道内镜检查术是直视食管肿瘤和活检的首选方法. 如果标准内镜不能通过恶性肿瘤高度狭窄处, 可用超细内镜, 其插入部直径仅为 5.3-6 mm^[5], 有 75% 的病例可通过狭窄段^[6], 并完成食管、胃的检查. 色素内镜通过喷洒卢戈氏碘液^[7-8]或美蓝^[9-10]使病变部位更明显, 易于观察, 而普通内镜却很难观察到.

1.2 活检和组织学检查 诊断性内镜检查应对疑似的病变部位进行活检. 通过标准活检发现食管或食管胃交界处癌的敏感率为 66-96%^[11-13]. 尽管 1 块活检即可, 但达到最好效果则需要 7-10 块活检组织^[14]. 大号活检钳能取到大块病变组织, 但并不能说明这样更有诊断意义^[15]. 另外, 细胞刷活检组织学检查能提高诊断价值, 因此建议狭窄严重的恶性病变进行刷检^[16]. 如果某处是临床高度怀疑的病变而未行活检和/或刷检, 那么超声内镜检查和/或无引导细针穿刺检查能够确诊^[17].

1.3 超声内镜分期 可根据美国癌症联合会和美国抗癌协会制定的 TNM 系统对食管腺癌和鳞状细胞癌进行分期(表 1)^[18-19]. 癌症的准确分期对疾病的预后和制定治疗计划具有重要意义, 并能减少医疗费用^[20-22]. 超声内镜对 T 分期准确率为 85%, 对 N 分期准确率为 75-80%,

比 CT 检查的准确率高^[23]. 超声内镜对 T3 和 T4 肿瘤分期比对 T1 和 T2 肿瘤分期更加准确. 运用高频(15-30 MHz)超声探头对小 T1 和 T2 肿瘤进行分期能将准确率 83% 提高到 92%^[24-27]. 超声内镜检查淋巴结时, 能发现恶性肿瘤的淋巴结浸润, 表现为边缘尖锐、圆形、大小超过 1 cm^[28-29]. 尽管这些个体的结果是可预知的, 如果同时具有这四种表现则诊断的准确率超过 80%^[28-30], 这种情况仅发生于少数病例. 对淋巴结进行细针穿刺提高了超声内镜对 N 期判断的准确率^[31-32]. 为取得最大敏感性, 至少要进行 3 次细针穿刺^[33].

表 1 食管癌 TMN 分类及分期标准

T: 原发肿瘤

- Tx 原发肿瘤不能确定
- T0 无原发肿瘤证据
- Tis 原位癌
- T1 肿瘤只侵及黏膜固有层或黏膜下层, 未及肌层
- T2 肿瘤侵及肌层
- T3 肿瘤侵及食管周围组织, 未及邻近器官
- T4 肿瘤侵及邻近器官

N: 区域淋巴结

- Nx 区域淋巴结不能确定
- N0 无区域淋巴结转移
- N1 区域淋巴结转移

M: 远处转移

- Mx 远处转移不能确定
- M0 无远处转移
- M1a 颈部或腹腔淋巴结转移
- M1b 其他远处转移

超声内镜可能对食管狭窄的诊断意义不大. 有 29% 食管狭窄的患者内镜不能通过^[34], 提示为进展 T 期病变^[35]. 内镜无法通过狭窄大大降低了 T 和 N 期诊断的准确率^[35-36]. 如果可能, 利用超声探头或 7.5 MHz 线控食管探头通过狭窄处并进行 T 和 N 分期^[25, 37-38]. 相比较而言, 食管狭窄经扩张后, 标准超声内镜可以通过. 这个过程有 0-24% 穿孔的危险性, 但在大部分患者中超声内镜都可以通过^[31, 35-36, 39-41].

化疗和放疗后所致炎症和纤维化使超声内镜不能准确的进行术后分期^[42-44]. 判定治疗后效果理想的方法是在放化疗后测量肿瘤的最大横截面^[43, 45]. 肿瘤最大横

截面减少50%以上表示肿瘤病理学上(经切除后证实)和临床疗效上的改善^[45-46]。

1.4 监测复发情况 当每个行食管癌切除术的患者有局部复发时应进行内镜检查,以作为病情的部分评价。如此,标准内镜能对40%患者的复发进行诊断^[47]。然而,肿瘤的复发经常发生在黏膜下,所以内镜检查时容易漏诊。超声内镜对癌症的阳性诊断率为75-100%^[47-48]。尽管超声内镜在肿瘤切除后能探查到复发,但对生存率是否有影响还未证实^[48]。

2 治疗

手术切除适用于所有能手术治愈的患者(T1N0或T2N0)。局部有进展性病变(T3或N1)的患者应在手术切除后进行放化疗^[49]。尽管食管腺癌不如食管鳞状细胞癌对放化疗敏感,但食管腺癌患者以术前多种治疗,其生存结果大提高^[50-51]。不幸的是,食管癌发展为进展期病变时才表现为吞咽困难,此时5a生存率不超过20%^[1]。

姑息治疗能改善大部分患者的吞咽困难,减轻疼痛,支持营养。目前几乎还没有随机对照试验或比较治疗的研究来评价最好的姑息疗法,因此,最佳的选择是以肿瘤的特征,患者的意向以及专家的意见为参考。

2.1 探条扩张术 对恶性狭窄可在或不在X线监视下,用经内镜气囊或经导丝引导的聚乙烯探条进行扩张。尽管大部分患者经扩张后标准前视内镜可以通过肿瘤狭窄段,但临床效果是短暂而不持久^[52]。因为Maloney盲法扩张术的穿孔率较高,对复杂的食管狭窄我们不建议应用此法^[53]。

2.2 放置支架 放置自膨式金属支架能够保持足够的管腔并减轻吞咽困难的症状,这已成为姑息疗法的主流^[54]。最初所使用的塑料支架在置入时有6-8%急性并发症发生,特别是食管穿孔。自膨式金属支架,替代了塑料支架,可在内镜和透视监控下将其置入事先定好的位置。这种装置减少扩张需要,甚至完全代替了扩张。一旦通过肿瘤狭窄段,支架推送器便释放支架,于是支架自动展开。熟练的操作者放置支架的成功率大于90%^[56]。尽管金属支架比塑料支架贵得多,但使用金属支架能大大减少急性并发症和死亡率^[55]。

食管金属支架置入后期并发症的发生率达20-40%。包括胸痛、支架移位、出血及瘘口^[57]。先前曾行放疗和化疗的患者出现严重并发症的危险更高^[58,59]。

放置食管上段和最远段的食管支架有很大困难。支架放置后可能导致异物感和呼吸不畅。若支架放置于食管胃交界处,则可产生难以处理的反流症状,并容易移位,产生溃疡和食物贮留。新近出现的一种不同于其他的Z型支架,在远端有类似风向袋的瓣膜能够有效地减轻严重的反流症状^[60]。对于需将支架置于贲门以上的患者,需要使用质子泵抑制剂进行抑酸,并保持直立或半直立姿势,包括将床头抬高大约30度。另外,放置支架的患者应调整生活规律,包括避免硬质和纤维

食物,注意食用液体和较软的食物,并且要求在直立时用餐。

食管气管瘘是食管癌非常严重的并发症,可导致呼吸困难。使用带膜支架进行治疗可封闭70-100%患者的瘘口^[61]。

2.3 电凝术和激光治疗术 热灼技术通常是对较短,外部生长的阻塞性肿瘤的姑息疗法。这些特征显示了临床疗效,包括单极和双极电凝术^[62],氩离子凝固术^[63],Nd:YAG激光治疗术^[64]。尽管价格便宜,但由于单极和双极电凝术不易控制而受到一定的限制^[62]。氩离子凝固术是一种非接触性治疗法,其原理是氩离子气化后产生电凝效应。然而,这种消融法用来治疗巨大阻塞性肿瘤太表浅而不能持续太久^[63]。高剂量的Nd:YAG激光能造成组织穿孔并能减轻巨大食管肿瘤。在内镜控制下,激光能使肿瘤组织凝固和气化。但激光较昂贵并需要较高技术支持^[64]。

2.4 化学烧灼术 化学消融可使用无水酒精,经济并易操作。此法是用硬化注射针将无水酒精等注射入食管癌处,与进行食管静脉曲张出血止血一样。组织坏死后能短暂减轻吞咽困难。所使用剂量还没有一定的标准,并且将硬化剂只注射入病变组织是比较困难的。术后常出现胸痛,缓解是短暂的,需要重复内镜检查^[65]。

2.5 光学治疗 光学疗法是将光敏药物-卟菲尔钠(porphimer sodium)注射并集中于肿瘤组织。在内镜引导下低剂量激光使肿瘤暴露于红外线下。光束能在敏感组织处产生光化学反应,产生具有细胞毒性的单氧原子,继而肿瘤坏死。红外线可造成很大的组织穿孔^[66]。光动力学疗法在技术上容易操作,由于选择性破坏的肿瘤组织,可以用来治疗几乎管腔完全阻塞的食管癌。光学疗法可以在化疗和放疗前或后使用。此法常用来限制肿瘤生长,防止以前放置过食管支架的患者再次狭窄^[67-68]。光动力学疗法的限制因素是卟菲尔钠半衰期较长,多种治疗的费用较高。卟菲尔钠灌注后在皮肤里可保留6wk,患者需避免阳光暴晒,有严重晒伤的风险。其他光动力学疗法的并发症包括胸骨下痛,咽喉痛,发热,胸腔积液和食管气管瘘。

2.6 内镜下黏膜切除术(EMR) 很少患者能发现早期食管癌,然而Barrett's食管的普查却可早期发现。诊疗中心所进行的食管切除的死亡率高达3-5%,发病率为18-48%^[69-70]。对于仅位于黏膜层的高度或中度分化的腺癌,其直径小于2cm并且有特定内镜下形态,内镜下黏膜切除术可使发病率和死亡率降低。研究显示,97%的早期食管癌患者经内镜黏膜切除术可免于临床随访。但在平均12mo的随访中,有14%的复发率或出现的腺癌。在最近一次非随机的研究中,食管鳞状上皮癌患者EMR术后或手术后,其5a生存率分别为77.4%和84.5%^[72]。另外,在这项技术被常规推荐前,需要进行长期随访的对比研究。大部分研究应用超声胃镜(EUS)来筛选行EMR的患者^[71-73]。

2.7 对比治疗试验 一项随机试验发现, Nd:YAG 激光为主的热灼治疗术与自膨式金属支架的置入术相比, 并不具有明显优势^[74]. 经热灼治疗患者的生存中位数高于放置支架, 但两组对症状的减轻都不太理想. 两组都出现了与治疗有关的明显的并发症, 热灼治疗组的平均住院时间和总花费要明显高于另一组. 光动力学治疗与激光治疗对症状的缓解有相同的效果, 而光动力学治疗更易操作, 患者更易耐受. 酒精注射与 Nd:YAG 激光的疗效相同^[75]. 另外一些研究表明, 金属支架优于热灼治疗. 一个前瞻性随机研究对比了支架和 Nd:YAG 激光治疗, 结果显示支架置入技术的成功率和对吞咽困难的改善比 Nd:YAG 激光治疗有较大的优势^[76].

总之, 食管癌有较高的发生率和死亡率. 内镜在诊断和治疗食管癌中起关键作用. 对可疑病变要进行多次活检和刷检. 超声内镜优于 CT 扫描, 他能精确地对病变进行分期, 并根据分期指导治疗, 从而提高疗效、降低花费. 大部分患者并不能治愈而需要姑息治疗. 通过探条扩张、烧灼肿瘤或置入支架可对吞咽困难的患者进行内镜下姑息治疗. 探条扩张可使患者症状得到短期的缓解. 肿瘤烧灼可应用酒精注射、激光、光动力学疗法, 与其他治疗有相同的疗效. 自膨式金属支架效果好于塑料支架. 姑息治疗方案的选择取决于肿瘤的特性、患者的意向和专家的意见.

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• 消息 •

科技论文产出排座次中国论文总数位居世界第五临床 医学类在国内名列前茅

健康报报道(记者张荔子) 12月7日, 2003年度中国科技论文统计结果显示, 我国科技论文占世界论文总数的5.1%, 继续处于美、日、英、德之后, 位列世界第五。其中, 临床医学67312篇, 在国内无论是论文数, 还是被引用次数都是最多的学科。

据介绍, 2003年度三种国际上具有影响的检索工具《科学引文索引》(SCI)、《工程索引》(EI)和《科学技术会议录索引》(ISTP)收录含有“中华人民共和国”的论文共93352篇, 比2002年增加15957篇, 增长率为20.6%。尤其是SCI论文数比上一年增长22.2%, 被引用篇数和次数分别增长了29%和39.3%, 表明我国论文影响力指标较数量增长得更快。

从SCI收录的论文可以看出, 2003年国际合作论文约占我国发表论文总数的23.6%, 比上年度增加2.2个百分点。涉及国家和作者最多的是在《英国癌症杂志》上发表的“关于酗酒、吸烟与肺癌的分析研究”一文, 共有30个国家和地区75个机构, 220位作者参与研究。

分类统计还排列出高等院校、科研、医疗等各类机构论文产出和被引用情况前20位。解放军总医院连续4年获全国医疗机构国内科技论文被引用数量第一名, 第四军医大学西京医院连续4年获全国医疗机构国内科技论文数量第一, 北京大学第一医院名列SCI收录论文第一(有关排名详见三版)。我国发表在国际高影响期刊、累积被引用次数最多的前10篇论文的第一作者有3位来自医院, 他们是阜外心血管病医院刘力生、中南大学湘雅医院夏家辉和上海第二医科大学瑞金医院牛超。

共有425种医药卫生类期刊进入2003年影响因子分类排序, 影响因子超过1的期刊有22种, 较2002年增加10种。值得一提的是, 在9种护理学类期刊中就有3种影响因子超过1。《世界华人消化杂志》影响因子2.924, 依然高居我国科技期刊首位。(2004-12-08)