

· 综述 ·

结直肠癌性肠梗阻肠道支架置入术治疗相关并发症的研究进展

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【摘要】 自 1991 年首次报道肠道支架应用于直肠癌性梗阻的姑息治疗后,内镜下肠道支架置入术在临床上得到广泛的应用。随着支架置入术治疗量的增加,其并发症问题也逐渐突显出来。肠道支架置入术后并发症包括穿孔、再阻塞、移位、出血、疼痛等,内镜医师应认识到这些并发症,并尽可能减少并发症的发生。本文将从支架成功率及并发症两方面进行阐述。

【关键词】 结直肠肿瘤; 支架; 癌性肠梗阻; 手术后并发症

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Research advances of complications of implantation of stent for treatment of malignant colorectal obstruction

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结直肠癌是全世界范围内最常见的癌症之一,约 5 个结直肠癌患者中有 1 个是以急性肠梗阻为首发症状^[1-3]。急性恶性肠梗阻如没有得到及时的评估与处理将会导致水电解质平衡紊乱、肠坏死、细菌移位甚至死亡。在过去,急诊外科手术是解除肠梗阻的常见方法,但其死亡率、并发症发生率高,而且术后造瘘率高,严重影响患者的生活质量。为解决这一问题,1991 年, Dohmoto 教授^[4]首次报道金属支架置入术作为直肠癌的姑息治疗方式,现多项研究表明,对于不能手术切除治愈的结直肠癌患者行支架置入术较急诊手术具有更高的生活质量,更快恢复经口饮食,更低的造瘘率,更短的术后住院天数^[5]。虽然姑息性支架置入术本身并不能使患者生存期获益,但是因其可以更早地行化疗从而间接使肿瘤分期下降的可能性增加^[6-7]。随后肠道支架逐渐作为术前过渡治疗手段在临床上应用,且较急诊外科手术具有更低的死亡率、并发症发生率、造瘘率以及更高的一期吻合率等优势^[8-10]。对于过渡性支架置入患者手术时机择期的研究较少,其最佳的手术时机不是很清楚,但是理论上最佳手术时机应该是允许更多的时间使得梗阻症状得到缓解,肠道水肿得到消退以及患者的一般情况得到恢复。因为时间太短,容易发生术后吻合口瘘, Lee 等^[11]的一项回顾性研究发现间隔时间 < 10 d 者术后吻合口瘘发生率明显高于 > 10 d 者 (20% 比 0)。最新一项研究发现,间隔时间 < 15 d 是术后并发症的独立危险因素,比值比 (odds ratio, OR) = 13.0, 95% 可

信区间 (confidence interval, CI): 1.010 ~ 167.0 ($P = 0.049$), 说明间隔时间 > 15 d 将会减少术后并发症。也有研究显示,间隔时间 > 18 d 将会增加复发的风险 ($OR = 2.6$, 95% CI: 1.1 ~ 6.5, $P = 0.037$)^[12]。随着操作量的增加,其相关并发症问题也逐渐突显出来。关于支架置入术后总体并发症发生率各研究结果不一,在 10% ~ 30% 之间^[13-14],这与研究类型、支架置入目的、研究人群不同有关,在姑息治疗组并发症发生率可高达 30%,而术前过渡组约 8.5%^[15-16]。最新一项 Meta 分析结果示,非覆膜支架较覆膜支架发生并发症的风险更低,相对危险度 (relative risk, RR) = 0.57, 95% CI: 0.44 ~ 0.74 ($P < 0.0001$),且这种获益只对晚期并发症特异 ($RR = 0.58$, 95% CI: 0.34 ~ 0.99, $P = 0.05$)^[17]。

一、肠道支架置入术成功率

1. 技术成功率:技术成功是指能够顺利的通过狭窄段并正确的放置支架至狭窄段,其成功率为 75% ~ 100%。技术失败的原因与梗阻程度、梗阻部位、操作者经验等有关^[18-19]。完全性梗阻因导丝通过困难较不完全肠梗阻技术成功率低;近端结肠由于操作途径长,难度大,技术上受到挑战。Williams 等^[20]通过肠道支架置入术的学习曲线探讨了技术成功率和操作者的经验关系,研究显示有经验的操作者技术成功率到达 90% 以上,且至少操作了 20 例支架置入术才认为是有经验的。

2. 临床成功率:临床成功是指支架置入术后 48 h 内患者

梗阻症状得到缓解,其成功率为 84%~100%^[19]。临床失败的常见表现为肛门仍未排便排气,或者腹痛腹胀仍得不到缓解,甚至腹痛加重,其原因有支架被大便嵌顿、术后穿孔、支架扩张不充分等,需立即内镜下干预或者外科急诊手术^[21-23]。

二、肠道支架置入术并发症

1. 穿孔:支架术后穿孔是严重的并发症,它会引起腹膜炎、败血症、弥漫性血管内凝血、多器官衰竭,甚至死亡^[24],其发生率为 1.6%~7.7%^[18,25-27]。按发生的时间可分为早期穿孔和迟发型穿孔;按是否肉眼观察到穿孔分为显著穿孔和微穿孔,微穿孔只有在病理检查时才能发现;按照临床表现可分为临床穿孔和亚临床穿孔,亚临床穿孔也称为沉默穿孔^[22]。有学者认为穿孔发生的可能原因有:支架的径向力对易脆的肿瘤组织的机械损伤、支架两端对肠壁的损伤以及导丝的过度操作^[28-29]。一项关于支架术后穿孔的 Meta 分析显示在手术当天发生穿孔率为 29%,前 3 d 发生穿孔率为 52.3%,术后 3 d 内应密切监测,一旦患者出现腹痛,应警惕穿孔的可能^[30]。发生穿孔的风险与术前扩张、使用贝伐珠单抗、年龄、操作者经验、梗阻程度等有关。Lee 等^[31]研究发现年龄>70 岁增加 3.276 倍穿孔风险,认为老年患者的肠壁更加薄弱以及肠系膜更加松弛导致了穿孔风险的增加。贝伐珠单抗是一种单克隆抗体,和血管内皮生长因子结合,从而阻止血管生成和抑制肿瘤生长,其常常被用在已经有远处转移的结直肠癌患者中。Manes 等^[32]对行姑息性支架置入的结直肠癌患者进行 3 年的随访,发现行贝伐珠单抗化疗的患者穿孔发生风险增加 19.6 倍。Hapani 等^[33]认为贝伐珠单抗引起消化道穿孔还可能与其剂量相关。贝伐珠单抗引起穿孔的确切机制不是很清楚,但可能与肿瘤侵犯结肠浆膜层发生坏死,局部缺血如血管栓塞、血管收缩,溃疡延迟愈合等有关。一项回顾性研究发现,梗阻的严重程度和内镜医师操作经验是发生穿孔的危险因素^[34]。一项 Meta 分析显示,行球囊扩张的患者较未行球囊扩张患者穿孔发生率更高($P<0.05$),对于穿孔导致肿瘤扩散从而影响肿瘤的长期预后仍然是不清楚的^[18]。Kim 等^[35]对支架组术后复发的患者资料进行了多因素分析,发现穿孔发生复发的风险是没有穿孔的 22 倍($OR=22.0, 95\%CI:1.3\sim362.9, P=0.030$),发生腹膜种植转移是未穿孔的 46 倍($OR=46.0, 95\%CI:2.0\sim1\,047.8, P=0.016$)。Avlund 等^[36]回顾性分析了 123 例术前过渡患者行支架置入术后发生穿孔和未穿孔患者的肿瘤长期预后,研究发现穿孔患者的五年生存率有更低的趋势、五年复发率有更高的趋势,但差异无统计学意义。最近一项回顾性研究显示,116 例术前过渡治疗的患者有 7 例发生穿孔,对 7 例穿孔患者随访 6~60 个月后无明显腹腔种植转移或者远处转移^[37]。Verstockt 等^[22]报告穿孔患者和未穿孔患者的生存率及腹膜转移率无差异。以上研究大部分是小样本或者回顾性研究,关于穿孔与肿瘤转移扩散的关系证据仍不足。发生穿孔后往往需要急诊手术。

2. 支架移位:支架移位发生率为 1%~10%^[18,22-23,38],其发生风险与支架类型有关。Mashar 等^[17]进行了一项关于覆膜支架和非覆膜支架的 Meta 分析,结果显示非覆膜支架发生移位的风险更低($RR=0.29, 95\%CI:0.17\sim0.48, P<0.001$),早期发生支架移位风险差异无统计学意义($RR=0.47, 95\%CI:0.21\sim1.06, P=0.07$),但覆膜支架可减少 89%的晚期支架移位($RR=0.12, 95\%CI:0.04\sim0.37, P=0.000\,2$)^[12],由此在临床上如结直肠癌患者发生急性肠梗阻无手术机会行姑息治疗时,可选择非覆膜支架。基于覆膜支架的移位率高这一特点,支架设计的改良如部分覆膜支架、支架两端扩大、支架内衬膜,以及不同形状的支架等增加其抗移位功能^[39-40]。放化疗后支架易发生移位,可能和肿瘤体积缩小有关^[41-42]。其他导致支架移位的原因有:梗阻程度、支架直径和长度不合适、内镜医师经验水平等^[34,43]。支架发生移位时常见的表现为阻塞症状如腹胀,如果出现剧烈腹痛或者出血时,需考虑穿孔或者结肠瘘管形成^[44]。无症状的支架移位可不需要处理,有症状的支架移位大部分行内镜下干预后可缓解。Choi 等^[45]认为支架移位后再次行内镜下治疗是安全有效的,且持续的临床缓解只取决于第 1 次支架置入的成功。

3. 支架阻塞:支架阻塞是最常见的并发症,发生率为 11.1%~16%,大部分发生在姑息治疗患者中,术前过渡组发生率为 0~1.1%^[22,46]。肿瘤的过度生长和向内生长是支架阻塞的主要原因,粪便嵌顿也有发生,应避免食用使大便干结的食物和泻药^[35]。一项 Meta 分析显示,非覆膜支架发生肿瘤向内生长的风险是覆膜支架的 5.99 倍^[47]。故为了减少肿瘤的过度生长和向内生长,临床上建议使用覆膜支架且支架两端至少覆盖无病变 2 cm 以上^[48]。重新置入支架是一种治疗支架阻塞的可行方法,Yoon 等^[49]探讨了支架阻塞后行第 2 次支架置入术的可行性和有效性,结果显示立即临床成功率为 75%,且与第 1 次支架通畅时间独立相关,第 2 次支架的通畅时间平均为 170 d,认为支架再置入是支架阻塞的有效治疗方法。Xinopoulos 等^[50]对因肿瘤阻塞支架的患者行肿瘤激光消融术,也取得满意的效果,是一种经济且操作简单的方法。

4. 其他:支架术后轻微出血在临床上较常见,据报道发生率为 8%~12%,出血与黏膜损伤、肿瘤的易脆性及溃疡形成有关^[51],大部分患者可自行缓解,少数需要输血治疗^[18]。腹痛或者肛门疼痛也常发生,但常常可以耐受或者口服镇痛药可缓解,极少数患者需要住院治疗。支架相关的死亡率一般为 0.4%~1%,穿孔是死亡的主要原因^[14],研究表明穿孔发生死亡的风险是未穿孔的 2.097 倍[风险比(hazard ratio, HR)=2.097, 95%CI:1.282~3.431, $P=0.003$]。突发心脏骤停致死也有发生^[48]。

三、结语

自 20 世纪 90 年代以来,内镜下支架置入术在结直肠癌急性肠梗阻中已经得到广泛的应用,其相关并发症也需引起临床医师的重视,尤其是术后发生穿孔与肿瘤长期结局的

关系,目前针对这方面大部分是小样本回顾性研究,期待更大样本的随机对照试验来验证穿孔与肿瘤长期结局的关系。

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结直肠上皮性肿瘤内镜下切除技术的发展现状

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【摘要】 热圈套器息肉切除术和内镜黏膜切除术是目前结直肠上皮性肿瘤内镜下治疗的标准方法, 但仍伴有相当大概率的不良事件, 由此诞生了诸如冷圈套器息肉切除术、内镜黏膜下剥离术、内镜全层切除术等新的内镜治疗技术, 本文就目前结直肠上皮性肿瘤内镜切除技术方面取得的进展进行了综述。

【关键词】 结直肠肿瘤; 上皮性肿瘤; 内镜下切除

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Development status of endoscopic resection of colorectal epithelial tumors

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结直肠癌是起源于结直肠黏膜上皮的恶性肿瘤, 是全球癌症相关死亡的主要原因之一。局部进展期结直肠癌患者的五年生存率约为 70%, 发生远处转移的晚期患者仅为 12%; 而大部分早期结直肠癌患者行早期治疗后均显示预后良好, 五年生存率超过 90%, 部分患者行内镜下微创治疗即可获得根治^[1]。内镜下治疗与传统外科手术相比创伤更小、愈合更快、住院时间短, 且术后患者的生活质量更高。因此, 普及和推广结肠镜检查及内镜下切除技术是实现结直肠癌早期诊断、早期治疗以及降低结直肠癌相关死亡率的有效手段。

热圈套器息肉切除术 (hot snare polypectomy, HSP) 和内镜黏膜切除术 (endoscopic mucosal resection, EMR) 是目前息肉切除的标准治疗方法, 优点为手术时间相对较短、并发症发生率相对较小^[2]。尽管已经在临床上得到了广泛的应

用, 但标准的 EMR 操作技术仍伴有相当大概率的不良事件, 如穿孔和出血。另外, 受限于器材及操作方式, EMR 在切除较大病变时, 可能无法实现完全切除, 使得术后复发及行二次手术的风险增高。初次手术后病变周围形成致密的纤维化组织, 会导致再次手术时黏膜下注射抬举不佳, 使病变更加难以治疗。因此, 为克服现有技术的缺点及局限性, 新的内镜下切除技术不断衍生。本文就目前结直肠上皮性肿瘤内镜切除技术方面取得的进展进行了归纳。

一、冷圈套器息肉切除术 (cold snare polypectomy, CSP)

传统 HSP 的原理是以圈套器对局部较厚组织进行横向切除, 通过即时血管凝固预防出血, 并对残留的异型组织进行热消融。然而, 其并发症的发生也常常与热损伤相关, 包括迟发性出血、迟发性穿孔以及热损伤导致的电凝综合征。为解决热损伤相关不良事件的发生, CSP 作为一种可行的替