

自膨式金属支架在结直肠癌伴肠梗阻中的应用

郭雅婕¹, 刘 帅², 邹馨阳³, 宋家伟¹, 李纪鹏^{1*}

¹西安医学院研究生处, 陕西 西安

²延安大学医学院, 陕西 延安

³曲靖市沾益区中医医院皮肤科, 云南 曲靖

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摘 要

结直肠癌(Colorectal cancer, CRC)是世界上第三大恶性肿瘤, 也是癌症相关死亡的第二大原因。结直肠癌合并梗阻的概率达20%, 常需要紧急处理, 以免发生穿孔、出血等严重并发症。在过去, 急诊手术是唯一可用的治疗方法, 虽然可及时切除肿瘤, 但却带来高死亡率和并发症率。自膨式金属支架(SEMS)自90年代问世以来, 已经越来越多地作为一种微创治疗手段用于结直肠癌梗阻的治疗中。本文就SEMS的发展以及在结直肠癌伴肠梗阻中的应用进行综述。

关键词

结直肠癌, 肠梗阻, 急诊手术, 自膨式金属支架(SEMS)

Self-Expanding Metal Stent in Colorectal Cancer with Intestinal Obstruction

Yajie Guo¹, Shuai Liu², Xinyang Zou³, Jiawei Song¹, Jipeng Li^{1*}

¹Graduate Office, Xi'an Medical University, Xi'an Shaanxi

²School of Medical, Yan'an University, Yan'an Shaanxi

³Department of Dermatology, Zhanyi District Hospital of Traditional Chinese Medicine, Qujing Yunnan

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Abstract

Colorectal cancer (CRC) is the third most common malignant tumor in the world and the second leading cause of cancer-related deaths. Colorectal cancer is associated with a 20% probability of

*通讯作者

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obstruction and often requires emergency management to avoid serious complications such as perforation and bleeding. In the past, emergency surgery was the only available treatment, which allowed for timely removal of the tumor but entailed high mortality and complication rates. Since its introduction in the 1990s, the self-expanding metallic stent (SEMS) has been increasingly used as a minimally invasive treatment in the management of colorectal cancer obstruction. This article reviews the development of SEMS and its application in colorectal cancer with bowel obstruction.

Keywords

Colorectal Cancer, Bowel Obstruction, Emergency Surgery, Self-Expanding Metal Stents (SEMS)

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1. 引言

结直肠癌(Colorectal cancer, CRC)作为一种消化道常见的恶性肿瘤,是世界上第三大恶性肿瘤,也是癌症相关死亡的第二大原因[1]。尽管目前强调癌症的早期筛查与早期诊治,但由于该疾病发病隐匿,进展迅速,仍有 7%~29%的患者以肠梗阻为首发症状就诊,其中超过一半的肿瘤梗阻发生在左半结肠[2]-[5]。肠梗阻的出现往往预示着结直肠癌的进展和不良预后。作为常见的内外科急腹症,有效缓解梗阻是临床医生首要的解决目标。传统治疗方法为急诊手术,术式包括:(1) 切除吻合并预防性造口,后择期关闭造口的二期手术;(2) Hartmann 术;(3) 术中结肠灌洗后切除吻合的一期手术。Hartmann 术一直被认为是该人群的首选治疗方法。但由于在急诊环境中难以进行充分的术前准备,且梗阻的存在导致严重的肠道扩张、肠壁水肿,通常伴随不同程度的水电解质失衡、腹腔感染等,同时多数患者为老年患者,一般身体状况较差,合并症较多,从而导致急诊手术的死亡率和术后并发症发生率远高于择期手术[6]-[9]。

自膨式金属支架(SEMS)经肛门置入可顺利通过结直肠梗阻的部位,有效地缓解梗阻症状,不仅适用于晚期姑息性患者,而且对于心肺功能差、不能耐受手术的患者也是良好的选择[10]。虽然肠道支架目前已广泛用于临床实践,但其相对于急诊手术的优势与禁忌证依旧是讨论的热点[11],尚无明确的结论与共识。本文通过结合国内外的研究结果以及专家共识对支架在梗阻性结直肠癌患者中的应用进行总结与阐述。

2. 结直肠癌肠梗阻的概述

研究表明,相比于无梗阻的结直肠癌患者,梗阻患者 5 年生存率较低,约在 31%和 42%之间[12]。在解剖学上,大致可将结直肠分为右半结肠、左半结肠和直肠。右半结肠肠腔直径较大、肠壁薄、血运丰富,主要生理功能为吸收水分及营养物质、促进粪便成型,其内容物多为非固态;大体类型多为隆起型,恶性程度相对浸润型低,发展较为缓慢,肿瘤可发展至较大体积后继发感染、出血等,患者常出现腹部包块、贫血及腹痛等症状。左半结肠肠腔相对较小,主要功能是储存粪便,肠内容物多为固态;大体类型多为浸润型,恶性程度高,沿肠壁浸润生长可堵塞肠腔,患者表现腹痛、便血且更容易出现肠梗阻症状。直肠癌主要表现为排便习惯及粪便性状改变。相比于右半结肠和直肠,病理类型主要以浸润型为主的左半结肠管腔相对较小,且粪便干硬,更容易出现肠腔环状狭窄和肠梗阻,临床上结直肠癌伴梗阻患者中 70%发生在左半结肠[13]。

3. 肠道支架的历史

自膨式金属支架(self-expanding metallic stent, SEMS)首先报道于1991年, Dohmoto 等人[14]对19例无法切除或远处转移的直肠癌伴梗阻患者行激光再通或扩张后置入自膨式金属支架以解除梗阻。Spinelli 等人[15]于1992年首次报道了内镜下放置自膨式金属支架(SEMS)治疗4例恶性直肠梗阻患者。此后随着不同类型的SEMS的发明和SEMS置入技术的快速发展, 其治疗目的并不仅仅局限于恶性结直肠梗阻患者的肠道姑息减压。到了1994年, Tejero 等人[16]首次尝试在2名结肠癌患者中置入SEMS, 以作为外科手术治疗前的过渡治疗, 并取得良好的手术效果。之后越来越多的人开始应用SEMS解除结直肠癌梗阻作为择期手术的一种过渡方式, SEMS的应用成为处理结直肠癌梗阻的一种非常有前景的治疗方式。

4. 肠道支架的类型及特点

4.1. 按照材料分类

近些年来, 随着支架的广泛应用, 为探寻更好的治疗效果, 不断有新的材料及科学技术用于开发制作肠道支架, 在支架的种类上, 单从材质方面进行分类, 主要包括塑料支架、生物可降解支架和金属支架。塑料支架的材料为聚乙烯、聚苯乙烯等毒性有机物质, 容易在人体内分解成有害物质, 损害患者健康, 并且易滑脱、易变形、内径小易堵塞, 目前多用于胆道、胰腺, 而肠道少用[17]。近年来, 生物可降解支架的研发取得了显著进展, 主要采用乳酸化合物作为原材料, 例如聚乳酸-羟基乙酸共聚物(PLGA)、聚乳酸(PLA)、聚丙交酯(PLLA)以及聚二恶烷酮(PDO)[18]。这些材料的降解产物不仅具有较低的肠道刺激性和较高的生物相容性, 而且能够被人体安全吸收和代谢, 从而减少了患者再次手术或肠镜检查的需求[19][20]。但其制作材料获取及加工技术难度大, 较为少用。金属肠道支架的材料包括不锈钢(即, Z-支架)(Cook Medical, 布卢明顿, 印第安纳州, 美国), Elgiloy 钴、铬和镍的合金(即, Wallstent)(Boston Scientific, Natick, MA, USA), 镍钛记忆合金(例如 Ultraflex (Boston Scientific, Natick, MA, USA)和 Alimaxx E (Alveolus, 夏洛特, NC, USA)支架)等[21]。其中, 最常用的制作材料为镍钛合金, 因其具有独特的形状记忆特性, 能够在肠道的自然蠕动下适应性地弯曲和变形, 从而保持肠道的通畅性[22][23]。

4.2. 按照有无覆膜分类

根据表面是否具有由有机材料构成的膜, 分为覆膜支架与无覆膜支架即裸支架。覆膜支架包括全覆膜支架和部分覆膜支架, 即支架的裸丝结构表面附着覆膜, 多为硅胶膜。既往研究[24]发现覆膜支架能够阻止肿瘤细胞通过支架的网眼侵袭, 具有抵抗肿瘤向内生长从而减少支架内再梗阻发生的优势。然而, Lee 等人[25]发现, 覆膜支架迁移率高于无覆膜支架, 因为覆膜的存在会导致与肠道肿瘤组织的摩擦相对较低, 进而引起支架的锚定能力减弱, 致使支架发生移位。为减少支架移位, 后改良开发出了支架两端裸露中间覆膜的部分覆膜支架, 稳定性得到提升。另有一些学者如 Mashar 等人[26]、Zhang 等人[27]、Yang 等人[28]开展的比较梗阻性结直肠癌使用无覆膜支架和覆膜支架的 meta 分析, 发现两种支架的技术和临床成功率并无明显差异, 但无覆膜支架的肠道通畅时间更长, 并发症更少, 支架转移率更低。因此, 2020年欧洲胃肠道内窥镜学会(European Society of Gastrointestinal Endoscopy, ESGE)建议肿瘤潜在可切除患者和支架置入为姑息性治疗患者使用无覆膜支架治疗恶性肠道梗阻[29]。

4.3. 其他类型

目前大部分管腔支架仅仅起到扩张支撑的作用, 还会机械性刺激肠壁引起增生、纤维化等病理改变; 而药物洗脱支架的发明可以在起支撑作用的同时进行局部治疗, 使药物在局部达到较高的浓度, 而不引起全身性反应[30]。搭载的药物主要为抗再狭窄及抗肿瘤的藥物, 如紫杉醇、5-氟尿嘧啶。在一项动物研

究中证实了负载 5-氟尿嘧啶(5-Fluorouracil, 5-FU)的支架治疗结直肠癌的有效性[31]。目前, 消化道药物洗脱支架尚处于研制及实验阶段, 其可能会成为不可切除结直肠癌治疗的新选择[32]-[35]。与药物支架理论相似的还有放射性支架, 即放射性粒子与支架结合, 支架由几乎不屏蔽射线的材料制成, 可直接对肿瘤进行靶向治疗, 明显提高了晚期肿瘤患者的临床缓解率, 是一个非常有前景的治疗手段[36] [37]。

5. 肠道支架的应用

5.1. 支架置入术作为限期手术的桥梁

结直肠癌合并梗阻的患者, 尤其是完全性肠梗阻者, 常需行急诊手术以解除梗阻同时尽可能切除肿瘤; 此时患者常无充足时间进行肠道准备, 手术死亡率和术后并发症发生率高; 且肠管条件差, 导致造口率高[38], 严重影响患者生存质量。支架临时置入后可迅速缓解梗阻, 恢复肠道功能, 同时给患者提供时间窗优化营养状况, 使临床医生能够明确临床分期, 尽可能提高限期手术的质量, 因此被誉为限期手术的桥梁[39]。

因此, 2020 年欧洲胃肠内镜学会(ESGE)建议在共同决策过程中将支架置入术作为手术的桥梁, 作为潜在可治愈的左侧梗阻性结肠癌患者的治疗选择, 作为紧急切除术的替代方案; 并且建议在可治愈的左半结肠癌患者中, 结肠支架置入术作为择期手术的桥梁时, 至切除的时间间隔约为 2 周, 但这个时间是基于低质量证据弱推荐[29]。但由于右半结肠支架置入具有挑战性, 为尽可能降低支架置入相关风险, 需要在具有资质的内镜中心来进行操作。

5.2. 晚期姑息治疗

很多导致梗阻的结直肠癌在得到诊断时已处于晚期, 无法切除的肿瘤以及肠道梗阻导致患者水电解质失衡、营养不良且高龄患者常合并其他疾病, 他们的选择往往是姑息治疗、解除梗阻。按照以往的治疗方法, 永久性造口可能是这些高风险人群的唯一选择。然而自肠道支架问世以来, 越来越多的研究表明肠道支架不仅可作为手术桥梁, 对于不可治愈的晚期梗阻性结直肠癌患者的姑息治疗也越来越被接受。2021 年美国胃肠病协会(AGA)在“恶性消化道梗阻的最佳管理方法”中建议对于不可切除的晚期恶性结肠梗阻患者, 自膨式金属支架置入术或者分流结肠造口术都是可取的[40], 但造口会对患者的心理健康以及生活质量带来负面影响。最近的一项针对无法治愈的恶性结肠梗阻的姑息性治疗研究中, 对比 202 例患者分别采取急诊造口术与支架置入术, 结果显示尽管支架置入的通畅性略低于造口, 但 1 年再干预率两组并无差异, 并且大部分患者的肠道支架有着足够耐久性[41]。可见, 晚期患者支架置入临床效果良好, 明显缩短了住院时间, 与造口相比未影响生存结局。

因此, 对于中晚期无法切除的结直肠癌伴梗阻患者, 早期使用肠道支架可以缩短住院时间、减轻患者痛苦、提高生活质量, 然而, 考虑到长期并发症管理和提高生存率, 则姑息性手术更有优势。对于一般情况差、无法耐受手术的患者, 肠道支架可作为首选。而对于身体状态较好、预期存活时间较长的病人, 发生支架相关并发症时手术可以作为二线替代治疗方法。

6. 总结与展望

近年来, 结直肠癌的发病率持续上升, 大多数医疗机构在处理伴急性肠梗阻的紧急情况时, 比较倾向于采用急诊手术, 这种方法往往伴随着较高的造口率、术后并发症率和死亡率, 并且肠造口会给患者带来生活和心理上的多重障碍。幸运的是, 随着肠道支架的出现为医生和患者提供了一种新的治疗选择。多项研究证实, 肠道支架置入成功率高, 安全性好, 并发症少, 创伤更小, 更加经济, 对生活质量影响更小, 它不仅可以作为晚期患者的姑息治疗手段, 也可以作为部分患者术前的减压治疗, 将原本的急诊手

术转变为更加安全的择期手术。

目前, 自膨胀金属支架(SEMS)在临床应用中仍面临诸多挑战和研究议题。首先, 需要深入探讨支架置入后对患者长期生存率的影响, 以及如何配合放疗和化疗等后续治疗。其次, 对于支架置入术在不同类型的结直肠癌患者中的效果, 尤其是在不同分期和不同部位的肿瘤, 也值得进一步研究。除此之外, 对于生物可降解支架和药物洗脱支架等新型肠道支架, 目前的研究和应用相对较少, 但这些新型支架的未来发展和应用前景广阔, 具有重要的研究意义和潜力。相信随着技术的持续进步和研究的深入, 新型肠道支架有望为结直肠癌患者提供更多的治疗选择和更好的治疗效果。

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