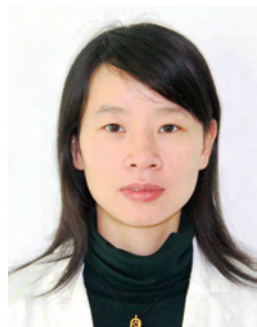


·述评·

癌性急腹症多学科团队综合处理 ——基于肿瘤放疗科思考

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【摘要】 癌性急腹症起病急、进展快、病因复杂、治疗困难、病死率高,需要多学科诊疗模式的参与。较单一学科诊疗模式,多学科综合团队(MDT)讨论可以使诊断更加准确,MDT会议能促进不同学科专家更好地进行沟通,选择最为合理的诊疗方案,提高诊疗的效率及质量。

良好的MDT可以涵盖疾病

诊断、评估和治疗的各个阶段,并给予良好衔接。本文将从肿瘤放疗科角度,探讨放射相关癌性急腹症的发生以及放疗在癌性急腹症治疗中的地位。常见放疗相关的胃肠恶性肿瘤急腹症包括出血、消化道梗阻和穿孔等。对于无法进行手术、内镜止血或栓塞治疗的胃癌急性出血患者,可考虑使用姑息性放疗作为癌性出血的止血治疗;姑息性大分割放疗可缓解胃癌所致梗阻症状。在急性下消化道出血的患者中,采用放射治疗作为止血手段的研究较少;对于发生肠梗阻的患者,在无法手术的情况下可考虑行姑息性放疗。癌性急腹症病因复杂、起病急、进展快、合并症多,应充分发挥MDT的作用,对于症状相对较轻、发展相对较为缓慢的患者,可谨慎选择放疗作为治疗手段,必要时急诊给予手术、介入等治疗,切不可盲目等待观察,延误治疗时机。

【关键词】 癌性急腹症; 多学科团队; 放射治疗

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DOI: 10.3760/cma.j.issn.1671-0274.2018.11.003

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【Abstract】 Malignant acute abdomen is a emergency with abrupt onset, rapid progress and often a complex etiology, presenting difficulties for treatment and high mortality. Therefore, multidisciplinary team (MDT) treatment modality is required. Compared with single-discipline diagnosis and treatment modality, diagnosis made from MDT discussion is more accurate, where specialists can improve efficiency and quality of the treatment through better communication. A good MDT can cover all stages from the diagnosis to the assessment and treatment of the disease, and combine them into a more coherent process. This article discusses the development of radiotherapy-related malignant acute abdomen and the role of radiotherapy in the treatment of malignant acute abdomen from the perspective of oncologic radiotherapy. Common causes of radiotherapy-related acute abdomen from gastric cancer include gastric hemorrhage, upper gastrointestinal obstruction and gastric perforation, while those of radiotherapy-related acute abdomen from colorectal cancer include lower gastrointestinal hemorrhage, intestinal obstruction, intestinal perforation and intestinal fistula. For patients with acute bleeding from gastric cancer that can not be treated by surgery, endoscopic hemostasis or embolization, palliative radiotherapy should be considered. Palliative hypofractionated radiotherapy has the advantage of reducing tumor burden in addition to relieving symptoms of gastric cancer. In patients with acute lower gastrointestinal hemorrhage, as relatively few studies have been established, short course of hypofractionated radiotherapy can be selectively applied. For patients with obstruction, palliative radiotherapy may be considered when surgical assessment is not feasible or tolerable. As malignant acute abdomen has rapid onset and progress, complex etiology and high rate of comorbidity MDT should be fully carried out. For patients with mild symptoms and slow development, radiotherapy can be applied with caution. Emergency treatment such as surgery and intervention should be given when necessary. Passive observation can result in missing the treatment opportunity and should be avoided.

[Key words] Malignant acute abdomen; Multidisciplinary team; Radiotherapy

癌性急腹症主要包括胃肠道穿孔、急性梗阻、消化道出血、肠套叠等,根据其发生的原因大致可分为由肿瘤自身原因和治疗相关两大类,本文将着重介绍与放射治疗相关的癌性急腹症。

一、癌性急腹症及放疗相关急腹症的概况

(一)胃癌

1. 胃出血:由胃肠道恶性肿瘤引起的非门脉高压性上消化道出血在总体上消化道出血中占 2%~4%,这一比例在亚洲人群中更高^[1-3]。在我国,恶性肿瘤所致的上消化道出血比例高达 10.9%~12.5%^[4]。上消化道出血是上腹部放疗最主要的剂量限制性不良反应(dose-limiting toxicity, DLT),当放疗总剂量低于 50~54 Gy 时,罕见放疗相关性上消化道出血。有研究认为,在门脉高压性胃病和胃窦血管扩张症的患者中,由于射线对于胃黏膜的直接损伤以及胃黏膜修复能力的下降,放疗相关性上消化道出血的发生率更高^[5]。

2. 上消化道梗阻:癌性上消化道梗阻主要见于贲门、幽门及十二指肠。食管下段肿瘤、贲门癌、远端胃癌、胰头癌、十二指肠癌、胃淋巴瘤以及该部位的转移性肿瘤均可能导致贲门及幽门梗阻的出现。由此导致的恶心、呕吐、营养不良以及脱水可严重影响患者生活质量,并严重限制进一步的抗肿瘤治疗^[6]。

3. 胃穿孔:胃癌所致自发性穿孔较为罕见,发生率约为 5%^[7-8]。放疗所致胃穿孔更为罕见,无论是术前放疗还是辅助放疗均鲜有报道。例如,在 MAGIC 研究中,共纳入 553 例患者,其中 250 例患者接受了术前放疗,无一例出现胃穿孔^[9]。在 SWOG-9008 研究中,一共纳入 559 例胃癌及食管胃结合部肿瘤患者,281 例接受了术后辅助放疗,同样没有报道胃穿孔的发生^[10]。而在 CROSS 研究中,仅有 1 例患者放疗后出现消化道穿孔导致死亡^[11]。导致胃穿孔的原因可能与肿瘤性溃疡的进展、在同步化放疗过程中肿瘤的迅速退缩坏死以及治疗过程中使用糖皮质激素等有关。在胃淋巴瘤的治疗过程中,由于手术的缺失和对放化疗的高度敏感,治疗过程中的胃穿孔尤其值得注意。

(二)结直肠癌

1. 下消化道出血:急性下消化道出血在整体消化道出血中约占 20%^[12-13]。相较于上消化道出血

而言,急性下消化道出血自发性止血率高、预后更好^[14]。在结直肠癌患者中,>90%的患者存在内镜下出血,37%~58%的患者合并显性消化道出血。放疗所致的直肠出血大多为前列腺癌、宫颈癌、子宫内膜癌等盆腔器官高剂量放疗后出现的迟发性损伤。前列腺癌放疗后最常见的肠道不良反应为便血,3级以上直肠出血的发生率为 2.7%~3.6%^[15-18]。这与处方剂量、直肠照射体积、既往盆腹腔手术病史、治疗方式、高龄、高血压等因素相关^[19-24]。研究认为,调强放疗的使用减少了肠道不良反应的发生,并可有效提高放疗剂量^[25]。因此在放疗计划的制定中,尤其应注意人群和治疗方式的选择以及包括直肠在内的器官保护。宫颈癌和子宫内膜癌的放疗包括外照射及腔内近距离放疗,有 5%~30%的患者治疗后可能发生肠道并发症,3级以上直肠出血的发生率约为 8%^[26-27]。迟发性肠道反应主要与肠道照射的体积、肠道平均剂量、直肠热点剂量、A 点剂量、分割方式、生物等效剂量以及正常组织的敏感性等相关^[27-29]。当患者存在炎症肠病、胶原血管疾病、既往盆腹腔手术病史以及盆腔炎症性疾病时,放射耐受性明显下降。

2. 肠梗阻、肠穿孔及肠痿:有 8%~29%的结直肠癌患者在初诊时发现合并肠梗阻^[30-32]。大多数梗阻部位在脾曲远端的肠道;某些盆腔肿瘤的外压性病变也可能导致肠梗阻。接受近距离放疗的患者发生肠穿孔和肠痿的概率更高。有研究显示,在前列腺癌接受近距离放疗的患者中,肠痿的发生率为 1%~2.4%^[33-34];而在直肠癌接受盆腔放疗的患者中,直肠狭窄发生率约为 5%,约有 5%的患者在放疗后出现小肠梗阻^[35]。出现狭窄及梗阻的患者中,有 9%~30%的患者最终需要通过手术治疗的方式来解决梗阻症状。总体来说,放疗所致的肠穿孔症状较为隐匿。根据 Ramirez 等^[36]报道,19%的放疗后肠穿孔患者可表现为急性腹膜炎,而仅有 9%的患者表现为严重的腹痛。这可能是由于穿孔部位纤维化及腹膜的包裹导致腹膜炎症状的局限,因而临床表现不典型^[37]。肠道的放射性损伤治疗很难,主要是对症处理,重在预防。妇科肿瘤放疗所致的严重迟发性小肠毒性(包括肠穿孔、梗阻及痿)发生率约为 5%^[34,38-39];同样,其发生率也与处方剂量、肠道照射体积、分割方式、放射技术以及是否同步化疗相关。因此,在设计放疗计划时应该慎重,尤其对于有肠粘连、既往盆腹腔手术史以及术后辅助治疗的患

者,应注意限制剂量,注意严格保护危及器官。

3.肠套叠:成人肠套叠罕见,48%的小肠套叠和43%的结肠套叠与恶性肿瘤相关^[40]。应注意鉴别。

(三)恶性胆道梗阻

胰腺癌、壶腹部癌、肝门部胆管癌以及胆道周围复发转移性肿瘤是导致恶性胆道梗阻的主要原因。恶性胆道梗阻可能导致凝血功能障碍、肝功能损伤以及胆管炎,继而可能诱发肝肾功能衰竭,因此,胆汁引流是该部分患者治疗的首要任务。有研究认为,无论采用何种方法,与无法重建通路的患者相比,重建胆汁引流通路的患者的中位生存时间均得到了显著延长(4.8~11.8个月比1.3~1.8个月)^[41]。

二、放疗在癌性急腹症治疗中的地位

(一)胃癌

1.胃出血:对于无法进行手术、内镜止血或栓塞治疗的胃癌患者,可考虑使用姑息性放疗作为癌性出血的止血治疗^[42]。在这一部分胃癌患者中,有54%~80%可以通过放疗达到止血的目的,采用的分割方式包括8 Gy/1F,30 Gy/10F,35 Gy/14F,40 Gy/16F等^[43-47]。有研究发现,在完成30 Gy或更高剂量的患者中,有91%的患者在1个月之后出血停止^[46]。来自日本的研究显示,73%的患者达到了止血的效果,中位止血时间为2(1~9) d,中位止血剂量为6(3~21) Gy,但有36%的患者在放疗结束后的治疗及随访过程中再次出现上消化道出血^[45]。而M.D.安德森癌症中心的研究认为,生物等效剂量 ≥ 41 Gy可能会带来更好的局部控制,尤其是对于T₄期的患者^[44]。

2.上消化道梗阻:相对于肠梗阻来说,胃癌所致上消化道梗阻发展速度较慢,患者可通过鼻胃管置入、肠外营养等方式暂时获得营养来源,因而有更充裕的时间接受内科治疗。针对癌性上消化道梗阻,患者可通过手术、消化内镜下支架置入等方式缓解梗阻症状,但放疗的优势在于,作为非侵入性的治疗,放疗可在缓解梗阻症状的同时,一定程度上降低肿瘤负荷。有研究显示,胃癌所致的上消化道梗阻患者接受姑息性大分割放疗治疗后,71%~81%可达到症状缓解^[43-44];而来自Tey等^[43]的研究显示,放疗后上消化道梗阻缓解的持续时间可达140 d,但值得注意的是,仍有一部分患者无法从放疗中获益,需从其他治疗方式中寻求解决。

(二)结直肠癌

1.下消化道出血:在急性下消化道出血的患者

中,采用放射治疗作为止血手段的研究较少,在患者体能状况允许、出血量大时应首先考虑手术治疗或栓塞介入治疗。部分小样本的研究认为,83%~86%的患者直肠出血症状可以通过姑息性放疗得到有效控制,症状控制持续时间可达5.4(0~29.4)月,但是仍有约33%的患者可能出现再次出血^[48-49]。因此,在充分评估患者出血量及出血部位的情况下,可有选择地采用放射治疗的方式。目前,下消化道出血的放疗大多采用短疗程大分割的方法,并且需要严密监测患者出血情况和血红蛋白变化,如放疗无法有效控制出血,应及时变更治疗方案。

2.肠梗阻:对于发生肠梗阻的患者,在外科评估无法进行手术或无法耐受手术时,可考虑行姑息性放疗。研究显示,在经过选择的合适患者中,使用姑息性放疗的手段治疗肠梗阻,可以使35%~88%的患者症状得到有效缓解^[50]。有研究认为,以姑息减症为目标的放疗,在20~30 Gy之间即可见到症状的缓解和控制,将剂量提高到46 Gy以上并没有见到更多的获益^[51];但仍应保证足够的处方剂量,研究显示,生物等效剂量 ≥ 40 Gy时局部控制更佳^[48]。一项来自挪威的前瞻性二期临床研究显示,采用5 Gy $\times$ 5次、序贯含奥沙利铂方案化疗结束后1个月,90%的患者主诉症状得到不同程度的改善,其中52.5%的患者在治疗前存在不同程度的肠梗阻^[52-53]。该研究认为,即便是存在局限性肠梗阻,在合适的时机选择合适的患者进行放疗,同样可能避免手术。尽管如此,仍有30%的患者在随后的治疗和随访过程中发生了肠梗阻复发,需要手术等其他方式进行治疗^[48]。

在以控制症状为主要目的的结直肠癌姑息性放疗中,大多数中心采用的是大分割短疗程的方式,其耗时短、费用低、对患者全身治疗以及短期内对急诊手术的影响均较小,不良反应大多为可耐受的1~2级^[54]。但需注意的是,在直肠癌的患者中,部分患者在新辅助或辅助治疗的过程中已接受过盆腔放疗,如进行再程放疗,3~4级的毒性发生率明显增加,并且应根据两程放疗间隔的时间合理地调整放疗剂量^[55]。在这部分患者中,尤其应当慎重选择姑息性放射治疗。

(三)恶性胆道梗阻

由于恶性胆道梗阻在短期内即可引起胆红素迅速升高,从而导致凝血功能障碍、肝肾功能损害及胆道感染等严重并发症,因而有效的胆道引流是

首要任务。无论是采用胆道支架^[56]还是经皮胆管引流的方式^[41,57-58],在胆汁有效引流的基础上,联合放射治疗,均有数据显示可以有效延长患者生存时间,延迟胆道再次梗阻,提高患者生活质量。

三、放疗在癌性急腹症多学科团队(MDT)诊疗模式中的价值

癌性急腹症病因复杂、起病急、进展快、合并症多,应充分发挥多学科团队(multidisciplinary team, MDT)诊疗模式的作用,使外科、肿瘤内科、肿瘤放疗科、影像科、介入科等多学科积极参与,提高诊断的准确率。对于既往曾经进行过放疗的患者,应充分考虑放疗相关性损伤,积极寻找病因。放疗医师在制定放疗计划时,应充分考虑放射相关损伤,谨慎选择治疗人群,确定合理的放射剂量及照射放射,充分保护危及器官,从而降低放疗相关性损伤,预防可能出现的放射相关癌性急腹症。MDT 是癌性急腹症进行综合治疗的基础,对于治疗方式的选择,治疗策略的制定,需要多个学科专家共同探讨。总的来说,由于急腹症起病急、进展快的特点,而放射治疗起效相对较为缓慢,因而在急腹症的治疗中受到很大限制。对于症状相对较轻、发展相对较为缓慢的患者,可谨慎选择放疗作为治疗手段,并且在治疗的过程中,需要严格监测患者病情变化及生命体征,根据病情的发展及治疗效果随时调整治疗方案。必要时急诊给予手术、介入等治疗,切不可盲目等待观察,延误治疗时机。

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(收稿日期:2018-09-06)

(本文编辑:朱雯洁)

·读者·作者·编者·

本刊对文稿中统计学符号撰写的要求

按 GB 3358-1982《统计学名词及符号》的有关规定,所有统计学符号一律采用斜体排印。常用:(1)样本的算术平均数用英文小写 $\bar{x}$ (中位数仍用 M);(2)标准差用英文小写 s ;(3)标准误用英文小写 s_x ;(4) t 检验用英文小写 t ;(5) F 检验用英文大写 F ;(6)卡方检验用希文小写 χ^2 ;(7)相关系数用英文小写 r ;(8)自由度用希文小写 ν ;(9)概率用英文大写 P (P 值前应给出具体检验值,如 t 值、 χ^2 值、 q 值等)。