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腔内近距离放射治疗食管癌的特点和作用

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摘要: 食管癌腔内近距离放疗是将放射源置于食管腔内进行放射治疗的一种方法, 它可以作为表浅性食管癌或复发性食管癌的主要治疗手段, 但更多的是将其作为局限性中晚期食管癌外照射后追加剂量照射的方法, 这样可以提高肿瘤控制率和患者的生存率, 对病变长度小于 5cm 或肿瘤局限于肌层的患者疗效更为明显。只要降低单次剂量、控制总剂量, 腔内近距离放疗的早期反应可以耐受, 后期并发症也可以得到控制。

关键词: 食管癌; 放射疗法; 腔内近距离治疗

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The characteristics and effects in the treatment of esophageal cancer with intraluminal brachytherapy

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Abstract: Intraluminal Brachytherapy(ILBT) is one method of radiotherapy by delivering the radiation resource into the Intralumen of esophagus. ILBT has been proposed as the effective method in the treatment for superficial cancer of the esophagus. More frequently, it has been utilized as a boost after external beam radiotherapy (EBRT) in inoperable patients with localized esophageal carcinoma. ILBT with EBRT may improve local control and survival. The effect were found to be strongly correlated with tumor less than 5 cm in length or tumor confined to esophageal wall. The patients may tolerate in acute effects, and late complications may be controlled with lower single dose and reasonable total dose.

Key words: esophageal cancer; radiation therapy; intraluminal brachytherapy

不能手术治疗的局限性中晚期食管癌, 放射治疗是有效的方法之一, 多数患者接受各种形式的放疗, 包括外照射和腔内近距离治疗(intraluminal

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brachytherapy, ILBT)。在美国的食管癌患者, 20.3%采用单纯放疗, 54%采用放化疗, 21%采用手术前或手术后放化疗, 仅有 8.5%的患者进行了 ILBT^[1]; 在日本, 也只有 8.8%的患者接受 ILBT^[2], 由此可见, ILBT 并未被临床上广泛接受。由于 ILBT 放射源的物理特性具有肿瘤剂量较高, 而食管周围正常组织放射剂量较低的特点, ILBT 成为提高食管癌局部照射剂量的有效方法, 但能否提高疗效临床上尚无定论, ILBT 的照射方法、剂量、疗效、并发症

等问题需要进一步探讨。

1 ILBT 方法的改进

1.1 放射源和施源器

经常应用的放射源有⁶⁰Co、¹⁹²Ir等,放射治疗是将它们做成针管状源,使用它们的 γ 射线。现在临床常用的放射源是¹⁹²Ir,是ILBT效果较好的放射源。

常规施源器为管状,直径一般为6~10mm^[3]。如果施源器直径太小(小于6mm),食管黏膜的剂量则明显加大,如果施源器直径太大(大于10mm),有可能增加食管损伤或穿孔的机会。使用带气囊的施源器,将气囊充气,可以减少正常食管组织的照射剂量。

1.2 ILBT 和外照射的序贯

如果X线摄片显示食管梗阻严重,患者进食困难,可考虑先行腔内放疗,尽快改善患者的进食状况^[4]。大多数情况是将ILBT放在一定剂量(35~60Gy不等)的外照射后进行,这时肿瘤厚度明显缩小,肿瘤剂量分布的均匀性有所改善,多数学者主张先外照射而后ILBT。

1.3 照射的长度

一般照射长度包括肿瘤两端1~3cm。如果外照射剂量较高,照射的长度应尽可能地短。照射的长度不能太短,否则会将黏膜下远处浸润的病灶遗漏。

2 ILBT 的剂量和剂量率

2.1 剂量参考点的确定

肿瘤剂量参考点通常定在距离导管中心轴10mm处^[3],但也有将肿瘤剂量的参考点定在黏膜下5mm^[5,6]或距离源中心12.5mm^[7]处。由于肿瘤浸润程度不同,所以采用统一的单一参考点是欠合理的,最佳方案是个体的治疗计划,即患者放好施源器后进行CT扫描,确定肿瘤的大小、外侵程度,通过治疗计划计算剂量分布并进行优化,同时确认施源器的位置是否准确^[8]。

2.2 以根治性治疗为目标的剂量

外照射结合ILBT,ILBT的剂量多采用4~6Gy/次,1次/周,共3~4次,总剂量小于20Gy。一般都采用分次治疗^[9,10]。Akagi Y等^[9]采用单次2.0~2.5Gy,其后期并发症较单次4~5Gy明显减少。最佳的分次剂量目前尚无一致的标准。考虑到疗效和并发症二个因素,在根治性放疗中,倾向于外照射

剂量应大于40Gy、腔内照射剂量应小于20Gy。

2.3 姑息性ILBT的剂量

对于晚期患者的姑息性治疗,Sur RK等^[11,12]推荐的高剂量率治疗剂量为:1次/周,8Gy/次,共2次;或6Gy/次,共3次。Vivekanandam S等^[13]采用低剂量率,剂量为36Gy/48h。

2.4 ILBT 的剂量率

ILBT分为HDR(高剂量率,>12Gy/h)和LDR(低剂量率,0.4~2.0Gy/h)照射,HDR照射治疗时间短,减少了护理和防护工作,减轻了患者的痛苦,成为当前发展的趋势。LDR照射治疗时间长,放射源不易固定,不易防护,增加了患者的痛苦,有逐渐被高剂量率超分割照射取代之趋势。

剂量率对放射生物效应有重要影响,低剂量率的长时间照射,早反应组织(如肿瘤)和晚反应组织(如某些正常组织)的损伤效应均下降,等效剂量升高,通常低剂量率照射的疗效和高剂量率相似,但后期并发症要低。现在HDR照射多采用较低的单次剂量多次照射,有较好的疗效和较低的并发症^[9]。本文ILBT的剂量率,除说明外,均是高剂量率。

合适的照射方法和剂量,应根据治疗目的和患者的具体情况来确定。如果是根治性腔内治疗,单次剂量要小(4~6Gy),分多次进行(3~4次);如果是姑息性治疗,单次剂量稍大(6~10Gy),分次少(1~2次)。为了减轻并发症,腔内照射应该在外照射后2~3周进行。

3 ILBT 的疗效

3.1 改善症状

ILBT主要是改善患者的吞咽困难和体重下降。Taal BG等^[4]研究发现,治疗后70%患者的进食困难可以快速得到缓解,66%患者的体重稳定或增加。Sharma V等^[12]治疗晚期和复发患者,48%的患者吞咽梗阻改善,中位生存期达7个月。Gaspar LE等^[14]报道,经过外照射和ILBT治疗,59%患者的吞咽困难得到改善,9.5%患者的体重增加,21.5%患者的体重稳定。

3.2 提高肿瘤的局部控制率

ILBT能够提高肿瘤的局部控制率,提高近期疗效,降低复发率。Yorozu A等^[7,9]报告,外照射加ILBT的肿瘤控制率为56%,明显高于单纯外照射,其中对肿瘤局限于黏膜下层、接受高剂量ILBT的

肿瘤控制率明显高于单纯外照射(60%比42%)和同步化疗(顺氯氨铂,5-氟尿嘧啶等);可以提高Ⅱ、Ⅲ期患者的肿瘤控制率,早期副作用可以耐受,后期并发症偏高。Someya M等^[15]报告,外照射后进行大于20Gy的ILBT,肿瘤控制率明显小于20Gy的ILBT高,分别为83%、26.5%。同时发现,外照射60Gy、ILBT 20Gy治疗长度小于5cm病灶,可以明显提高肿瘤控制率。Nishimura Y等^[16]报告,外照射结合ILBT治疗表浅食管癌的近期肿瘤控制率为100%,3年控制率(85%)明显高于单纯外照射(45%)。

3.3 提高患者的生存率

ILBT能否提高长期生存率,目前的临床研究结果不尽相同。Okawa T等^[6]报告,外照射结合ILBT比单纯外照射可提高5年生存率(38%比27%),特别当病灶长度小于5cm时疗效更加明显(64%比31.5%)。Someya M等^[15]报告,ILBT可明显提高病灶长度小于5cm患者的5年生存率。Maingon P等^[17]报告,单独用ILBT治疗表浅性或复发性食管癌的1年和3年生存率分别为76%和14%,显示ILBT可以单独治疗表浅性或复发性食管癌,疗效与外照射相似。Nishimura Y等^[16]报告,ILBT结合外照射可提高表浅性食管癌的3年生存率。但是,Nemoto K等^[18]报告,ILBT结合外照射治疗表浅性食管癌的5年生存率无显著差异。在回顾性非随机分组的研究中,尚不能完全肯定ILBT结合外照射的疗效高于单纯外照射,日本学者已经开始前瞻性临床试验,以确定食管癌放疗的最佳方法。

4 ILBT的并发症

ILBT的主要并发症有放射性食管炎、食管溃疡、食管良性狭窄和穿孔等,最常见的并发症是放射性食管炎,表现为吞咽痛、胸背痛,轻者对症处理症状能够缓解,重者可持续较长时间,甚至出现溃疡,其发生与腔内照射的剂量和次数有关。

食管溃疡是腔内照射后的主要并发症,其发生率为7%~22.6%^[4,7],与外照射相似^[6,15],但有作者报告比单纯外照射要高,单次剂量大于5Gy、总剂量大于20Gy,食管溃疡明显增加^[7,18]。Yorozu A等^[7]发现,腔内照射食管溃疡的发生率和照射剂量成正比,剂量24Gy时食管溃疡发生率为80%。Hishimura Y等^[16]报道外照射后高剂量率腔内照射4Gy,2~3

次,治疗21例食管癌,食管溃疡发生率为15%。

ILBT后食管良性狭窄往往与食管溃疡同时或异时在同一患者发生,并与肿瘤长度、肿瘤软组织阴影、食管炎、管腔直径及管壁硬度有关,发生率为6.4%~16%^[7,11,12,17]。严重的食管狭窄会影响患者的进食,可采取腔内扩张术或支架植入来缓解症状^[13]。

食管大出血、穿孔、食管瘘是ILBT后较严重的并发症,但其发生率一般比较低。食管瘘的发生率为1.8%~12%^[9,12]。由于ILBT后重度食管炎、食管溃疡的发生率明显高于外照射,而未明显提高疗效,所以ILBT并未被临床上广泛接受。

外照射结合ILBT同步化疗(顺氯氨铂,5-氟尿嘧啶等)可以提高肿瘤控制率和患者的生存率、降低复发率,早期反应中等,患者可以耐受,但增加了后期重度并发症^[9,10,14,19],应避免化疗和ILBT同时进行。增加照射剂量不能提高局限期中晚期食管癌的疗效^[3,20],反而明显地增加了放射性损伤,最好的办法是术前放化疗,然后争取手术治疗。对外照射40~50Gy后食管病灶消退或基本消退的患者,可考虑继续外照射或ILBT,疗效较差的患者,则应尽量手术治疗,然而,这个方案是不是最佳方法有待临床试验的验证。

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瘤的放射性碘治疗开辟崭新的领域。因此,如何有效地控制 NIS 基因的表达,增强放射性碘治疗的效果,减少放射性碘带来的副作用将是今后研究的重点。

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