

胸段食管癌根治术后复发病规律的临床研究

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摘要 食管癌恶性度高,手术治疗仍是其治疗主要手段,即使行广泛三野淋巴引流区域清扫仍有较高复发比例。对于局部晚期、淋巴结转移或伴有其他不良预后因素者术后放疗可以降低胸腔内复发,提高部分患者生存率。然而,多组关于术后预防性放射治疗的前瞻性研究均显示放疗范围不统一。胸段食管癌根治术后主要的复发部位为上纵隔淋巴结区和锁上淋巴结区,影响其复发的因素主要包括手术术式、肿瘤部位、肿瘤侵犯深度、术后淋巴结是否转移以及转移数量等。根据食管癌根治术后的复发规律合理进行术后放射治疗的靶区设计,对提高食管癌根治术后患者的局控率,进而改善生存率具有重要的临床意义。

关键词 胸段食管癌 复发 放射治疗靶区

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Clinical Studies of Relapse Pattern in Patients with Carcinoma of Thoracic Esophagus after Surgery

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Abstract Esophageal carcinoma is a highly aggressive tumor. Surgical therapy remains the mainstay of treating locally advanced diseases. However, the rates of local recurrence of the disease are high after a three-field lymphadenectomy (cervical, mediastinal, abdominal) alone in patients with carcinoma of thoracic esophagus (CTE). Postoperative radiation therapy after radical operation of the esophageal cancer can reduce the intra-thoracic recurrence rate and improved the overall survival for patients with cancers of locally advanced stage, positive nodal disease and poor disease-related prognosis, such as the diseases with three or more positive lymph nodes, stage-III/IV, and large or deeply invasive tumors. However, the radiation fields are different in the previously prospective randomized trails, and the optimal target volume of the postoperative radiotherapy for treating CTE is still controversial. Studies of the recurrence of thoracic esophageal squamous cell carcinoma after radical surgery would provide instruction for deciding the target volume of postoperative radiotherapy. The pattern of recurrence in surgically treated patients with thoracic esophageal squamous cell carcinoma is mediastinal lymph nodes and supra-clavicular lymph nodes. The factors involved in the relapse include operative approach, site of tumor, depth of tumor infiltration, and nodal metastasis after operation, and the number of the metastasized nodes. The characters of recurrence after esophagectomy will provide an important reference to design the radiotherapeutic target volume. Both local control and survival rate of the CTE patients will obtain benefit from a proper target volume of the postoperative radiation.

Key words Carcinoma of thoracic esophagus; Recurrence; Radiotherapeutic target volume

据2010年流行病学调查资料显示,肺癌、胃癌、结直肠癌、肝癌、食管癌等占全部恶性肿瘤发病的75%以上,食管癌的发病率位列第6,但死亡率却位列第4位^[1]。在美国,2012年报道食管癌发病例数为1.746万,而死亡人数高达1.507万^[2]。单一手术治疗的患者5年生存率为23%~52%,术后复发为其治疗失败的主要原因,复发率在9.7%~51%之间,远处转移发生率在15%~30%之间^[3-5]。因此食管癌的治疗逐渐转变为放化疗结合手术的综合治疗。目前,对于食管癌术后是否放射治疗,多个研究显示对于局部晚

期及有不良预后因素者术后放疗可降低局部复发率,提高生存率^[6-9]。本文探讨了食管癌根治术后的复发病规律,为食管癌术后放疗靶区的确定提供临床依据。

1 胸段食管癌根治术后主要复发的部位

胸段食管癌根治术后主要复发的部位为纵隔淋巴结区和锁骨上淋巴结区。周纯武等^[10]在食管癌术后使用CT随诊过程中发现,术后复发的主要区域为颈部淋巴结区和上纵隔淋巴结区。刘冠等^[11]报道111例胸段食管癌根治术后复发有一定规律,复发部

位主要是双侧锁骨上淋巴结(33.3%)、气管食管沟淋巴结(27.9%)、上纵隔淋巴结(19.8%),吻合口复发约10%,而瘤床复发仅2.7%。

2 不同术式对复发的影响

食管癌术式目前主要包括以下两类,一类为经膈食管切除术和经胸腔食管癌切除术,手术切除范围小,不进行系统淋巴结切除;另一类为食管根治术及广泛淋巴结清扫术,包括食管癌根治性两野切除术和三野切除术。不同术式术后区域淋巴结复发及生存也存在差异。多篇文献报道,食管癌术后局部复发率为17.0%~41%,远处转移率为13.1%~46.2%^[12-13]。Fujita等^[14]比较了食管癌根治性两野切除术和三野切除术之间的差别,发现上、中段食管癌有淋巴结转移时行三野清扫术式的生存时间更长。Kato等^[12]比较三野和两野切除术的复发率和生存率,入组均为T₃患者,其中进行三野切除50例,5年总生存率为36.8%,17.0%患者出现区域淋巴结复发;行二野切除者为100例,5年总生存率为22%,37.8%患者出现区域淋巴结复发。术后复发部位显示,两野主要复发部位为上纵隔和锁上。因此,对于食管上段或局部晚期的患者,三野根治术可能较两野局部清扫更为彻底。

3 肿瘤部位对术后复发的影响

不同部位的肿瘤术后复发模式有所不同^[15-17]。胸上段失败的主要形式为胸腔内复发,随肿瘤部位的下移,胸腔内复发所占比例逐渐下降。因此无论肿瘤位置,胸腔内的胸腔内复发是失败的主要原因。对于上、中段的肿瘤,锁骨上淋巴结转移是其失败的另一个主要原因,比例约30%,即上纵隔及锁骨上淋巴结转移是食管中、上段癌术后复发的主要部位。腹腔淋巴结转移因不同部位的食管癌有所不同,Cai等^[16]报道胸下段癌腹腔转移为36.2%,明显高于胸中、上段癌的转移率,且胸下段癌术后肝转移率较高。章文成等^[17]对不同段食管癌术后复发构成比分析,其结果显示胸上段失败的主要形式为胸腔内复发,随肿瘤部位下移其比例逐渐下降,但胸下段食管癌仍有42.9%因胸腔内复发造成治疗失败。

4 T分期对术后复发的影响

多个研究表明,不同T分期对术后是否复发有明显的影 响。Visbal等^[18]分析220例Ivor Lewis术后患者复发情况,结果发现T₀者无复发,随着肿瘤侵犯程度加深复发率逐渐升高,T₁者术后复发率为45%,T₂者则高达67.5%,T₃、T₄分别为68.9%和100%。对不同分期术后复发情况进行分析,也得到相似的结果,0、I期无复发,II A期复发率为41.6%,II B期为72.6%,III期为80.7%,IV期为100%。Nakagawa等^[13]研究

发现,食管癌三野清扫术后,T₁+T₂术后复发比例为17/73,而T₃+T₄术后复发比例则高达57/98($P<0.0001$),局部复发也是如此,T₁+T₂术后局部复发比例为9/73,而T₃+T₄术后局部复发比例则高达21/98($P<0.0001$)。因此随着肿瘤浸润范围加深,食管癌根治术后复发率也逐渐增高,局部晚期为食管癌术后复发的高危因素。

5 术后转移淋巴结数对复发的影响

Visbal等^[18]分析发现,术后淋巴结阴性者复发率为28.9(21/73),淋巴结阳性者复发率为78%(115/147),差异有显著性($P<0.001$)。多篇文献^[3-4,18-19]研究发现,术后淋巴结阴性者复发率17.6%~37.9%,而淋巴结阳性者复发率为52.5%~78%,因此术后淋巴结阳性患者为复发高危因素。

进一步研究发现,术后转移淋巴结数目对复发也有一定影响(表1)。Baba等^[3]分析了108例胸段食管癌病例,随访发现49例复发,最主要的复发区域为上纵隔(包括颈胸交界)29例和肺转移11例,腹腔淋巴结复发8例,吻合口1例。作者将49例病例根据手术阳性淋巴结个数分成无淋巴结转移组、1~5枚淋巴结转移组、≥6枚淋巴结转移组,发现随着阳性淋巴结个数的增加,患者复发几率增加,差异有显著性($P<0.01$),并且各组复发的平均时间也存在显著性差异(24个月 vs. 18个月 vs. 8个月, $P<0.01$)。Bhansali等^[4]报道,手术时淋巴结清扫较彻底的部位如食管旁、后下纵隔、贲门旁、胃左区,术后该区域淋巴结复发几率较低,而清扫困难的区域如双锁上、颈段食管旁,术后淋巴结复发几率相对较高。另外,手术切除淋巴结的数目对复发生存也有明显影响,Rizk等^[20]通过对4627例行单纯手术食管癌患者术后复发生存分析,推荐食管癌根治术患者,pT₁者术中至少清扫10枚淋巴结,pT₂者至少清扫20枚淋巴结,pT₃/T₄者至少清扫30枚淋巴结。

6 食管癌术后吻合口的复发

Gao等^[21]研究发现食管癌术后标本病理大切片检查发现上下扩散距离一般<3 cm。章文成等^[17]对食管癌单纯手术复发患者进行分析发现,术后肿瘤最小切缘<3 cm者吻合口复发概率明显增加。Mariette等^[22]报道了439例食管癌R0切除术后5年生存率为41%,230例出现复发,其中局部复发为12.1%,区域复发为20.5%(颈3.6%,纵隔14.8%,腹部2.1%),远处转移为19.8%,53例发生吻合口复发,其中胸上段食管癌吻合口复发率为9.7%(6/62),胸中段为14.7%(36/245),胸下段为8.3%(11/132)。然而,Xiao等^[23]对275例行单纯手术的食管癌患者吻合口复发进行分析时发现,以胸上段癌吻合口复发率最高,为16.7%(5/30),胸中段和胸下段癌吻合口复发率

分别为3.1%(5/161)和7.7%(4/52),明显低于胸上段($P=0.011$)。总之,术中切缘距离小以及肿瘤位于胸上段为吻合口复发的高危因素。

表1 不同淋巴结转移个数患者的术后的失败率

Table 1 The recurrent rate of thoracic carcinoma of esophagus after esophagectomy with different number of lymph node metastasis

作者	淋巴结(枚)	例数	复发率(%)	P
Baba, et al ^[3] , 1994	0	28	29	<0.001
	1~5	50	42	
	≥6	28	71	
Smit, et al ^[19] , 2010	0	87	37.9(5年)	<0.001
	≥1	115	72.3(5年)	
Bhansali, et al ^[4] , 1997	0	6	23	<0.01
	1	7	33	
	1~4	10	48	
	≥5	16	73	

综上所述,胸段食管癌术后常见复发部位为纵隔淋巴结区和锁骨上淋巴结区,在考虑不同术式进行照射野设计时,应注意将手术未清扫区域或不易彻底清扫的部位纳入照射野,对于胸上段或胸中段淋巴结阴性的食管癌术后患者,其高复发部位为上纵隔和锁骨上区,对其照射野设计应该包括该部位,而对于胸中段或胸下段淋巴结阳性的患者,全纵膈及腹腔淋巴结均为高复发部位,术后放疗应重点考虑。总之,手术术式、肿瘤位置、术后T/N分期及淋巴结转移个数对术后复发部位及几率有重要影响,但根据术后复发规律所确定的术后放疗的适应症以及放疗的靶区范围是否合理,尚需要临床研究进一步证实。

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