

## • 综述 •

## 经内镜黏膜下剥离术在早期胃肠道肿瘤中的应用

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**摘要:**胃肠道恶性肿瘤是造成人类死亡的主要病因之一,提高消化道恶性肿瘤患者的生存率及生存质量的关键在于早期诊断和治疗。近年来,随着消化道内镜诊治技术的不断发展,出现了既可以达到肿瘤根治目的,又可以提高患者生存质量的内镜下治疗方法。经内镜黏膜下剥离术(ESD)作为一种新兴的内镜下治疗技术,因其治疗安全性高、效果好,在早期消化道肿瘤中的应用已逐渐开展。

**关键词:**经内镜黏膜下剥离术;早期胃肠道肿瘤;治疗

消化道恶性肿瘤是造成人类死亡的主要病因之一,每年全球经消化内镜明确诊断的新发病例达35万例,同时约有19.7万例因此而死亡<sup>[1-2]</sup>。由于目前除外科手术等方法切除病灶外,尚无其他有效的根治措施,而越早期的病灶根治率越高,故早期诊断和治疗是改善患者预后的重要手段之一。对于一些早期无转移肿瘤患者,理论上行局部切除即可达到治疗目的,行传统外科手术治疗对于这些患者而言已属创伤过大,被称之为“过治疗”。

近年来,随着消化内镜诊治技术的不断发展,出现了经内镜黏膜下剥离术(ESD)等一系列安全有效的内镜下微创治疗早期消化道肿瘤的方法。行ESD治疗之前先行超声内镜等检查判断病灶浸润深度及有无淋巴结转移。治疗前,患者需做好充分胃肠道准备。治疗时,先行内镜下色素染色等方法确定病灶范围,在病灶周围做好标记(可用针状电刀等),然后行黏膜下注射使黏膜层隆起,随后用针状电刀等将隆起的黏膜层切开一小口,紧接着用IT刀插入小孔切开黏膜,沿着标志好的边界将黏膜逐渐切除,继续注射,最终将整块病灶切除。IT刀末端的陶瓷球可限定切除的深度从而能有效地避免穿孔的发生。随着科学技术的不断发展,为增加操作的简便性和安全性,除了最先出现的IT刀外,其他还有如钩刀、折刀、三角刀等相继出现,为临床操作提供了更多的选择。与传统手术治疗早期消化道肿瘤相比,ESD具有创伤小、安全性高、治疗效果佳、患者依从性好、治疗成本低、可完整切除早期病灶并对肿瘤进行分期等优点,因而倍受广大医务工作者和患者青睐。对于一些高龄及合并有其他较严重疾病而无法耐受常规外科手术的患者,亦可进行ESD治疗<sup>[3]</sup>。在日本,该技术已较为成熟,在临

床中有着较为广泛的应用。目前ESD已被成功地应用于胃、食管以及结直肠等早期消化道肿瘤的治疗中。

### 1 ESD在早期胃癌中的应用

EMR和ESD最早被应用于早期胃癌的治疗中,因此该技术在治疗早期胃癌方面较为成熟。由于EMR及ESD均为局部微创治疗,故肿瘤的浸润深度及是否有淋巴结转移等已成为是否可行该项治疗的关键因素。Gotoda等<sup>[4]</sup>对5265例经手术切除并清扫至R2站淋巴结的早期胃癌病例进行了统计分析,结果发现2300例局限于黏膜层内的病灶(其中1230例为小于3cm的分化型腺癌,929例为大于3cm的分化型腺癌,141例为小于3cm且无溃疡形成的未分化腺癌)均无1例发生淋巴结转移,145例小于3cm的分化型微小浸润性早期胃癌(肿瘤侵及黏膜下层小于500 μm)亦未发现淋巴结转移。基于大量研究结果,综合常规手术的风险考虑,几乎不发生淋巴结转移的早期胃癌类型被列为EMR的适应证:(1)病理特征为高分化或中分化腺癌,乳头状腺癌的黏膜癌;(2)直径小于2cm的Ⅱa型病变;(3)直径小于1cm的Ⅱb、Ⅱc型病变;(4)内镜及病理检查无溃疡及溃疡疤痕形成者;(5)无静脉和淋巴结转移者。一般认为病理特征为低分化腺癌或印戒细胞癌的早期胃癌,直径大于2cm的Ⅱa型病变,直径大于1cm的Ⅱb、Ⅱc型病变,以及黏膜下癌因其淋巴结转移发生率较高而不推荐行EMR治疗<sup>[5]</sup>。与EMR相比,ESD可切除的病变范围增大,对肿瘤的切除率明显高于EMR。亦有其他临床研究表明,内镜下治疗早期不伴淋巴结转移的胃癌是安全有效的<sup>[6]</sup>。因此在日本,EMR及ESD临床上已成为治疗早期胃癌的首选方法之一。

由于ESD切除病灶范围较大,其操作时间亦相应延长<sup>[7]</sup>,同时,因切除病灶大,ESD治疗过程中出现出血、穿孔等并发症的概率也相应增加,分别为25%和5%<sup>[8]</sup>,但大多可通过内镜下治疗,如局部喷

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洒凝血酶,金属夹夹闭,乙醇注射等得以控制<sup>[9]</sup>。为减少ESD操作引起的出血及穿孔的并发症,近来Fujishiro等<sup>[10]</sup>研究发现,用一种由透明质酸、10%三酰甘油及5%果糖溶液混合而成的高分子物质在ESD治疗过程中作为黏膜下注射液,能减缓吸收而明显延长黏膜层隆起的时间,可在增加治疗效果的同时减少并发症的发生。

ESD治疗早期胃癌可以切除最大直径约100 mm的病灶,但要求不伴有淋巴结转移,因此在作ESD治疗前,需进行超声内镜等检查以明确。近来有学者对一些有可疑淋巴结转移的患者行ESD+腹腔镜淋巴结切除(LLND)治疗,为今后微创治疗早期胃癌而伴有淋巴结转移的患者提供了一个可供选择的方法<sup>[11]</sup>。

此外,尚有ESD治疗复发性胃癌的研究,认为只要病灶局限于黏膜内,就可通过ESD将其完整切除<sup>[12]</sup>。

## 2 ESD在早期食管肿瘤中的应用

随着EMR在治疗早期胃癌中日渐成熟,有学者开始将其应用于早期食管癌的治疗中。Noguchi等<sup>[13]</sup>使用EMR治疗了33例早期食管癌患者,并与外科手术在治疗的安全性、患者预后及生活质量等方面进行了综合比较,发现对局限于黏膜内的病灶,更适合行EMR治疗。Maish等<sup>[14]</sup>通过临床研究,认为EMR也可用于临床食管腺癌浸润深度的评估。之后,随着ESD的出现,亦被引入早期食管肿瘤的治疗中。借鉴ESD治疗早期胃癌的方法,Fujishiro等<sup>[15]</sup>对43例、58处局限于黏膜内的早期食管鳞癌的病灶行ESD治疗,所有病灶都通过ESD达到整块切除,切除病灶经组织学证实为R0切除者占78%(45/58),治疗中没有发生严重的出血,有4例(6.9%)在治疗过程中出现了穿孔,但均通过内镜下治疗得以控制,9例(16%)出现食管狭窄而在术后需要进行气囊扩张治疗。结果显示,有31例的40处病灶在平均17个月的随访期内均无复发,达到了完全切除的标准。此外,食管腺癌多数是在Barrett食管的基础上演变而来,处于胃食管交界处。Kakushima等<sup>[16]</sup>对胃食管交界处局限于黏膜内的肿瘤进行ESD治疗,证明同样是安全有效的。

由于解剖因素,食管肿瘤行外科手术的创伤及危险性均有所增大,因此对于早期不伴有转移的患者,ESD治疗在一些临床应用中已被证实是相对安全有效的。但迄今为止,ESD在早期食管肿瘤中的应用尚无大量临床资料,并且容易发生狭窄等并发症也是需要我们加以注意的。不过,相信随着经验的积累及技术的发展,ESD将会成为较好的微

创治疗早期食管肿瘤的选择之一。

## 3 ESD在早期结直肠肿瘤中的应用

基于ESD可以完整切除黏膜内病灶,且早期分化较好的肿瘤发生淋巴结等转移的概率极小,因此有学者将其引入早期结直肠肿瘤的治疗中。但由于结直肠解剖结构较胃食管有较大差异,其肠壁较软较薄,使治疗过程中发生穿孔等并发症的可能性有所增加;同时因结直肠内细菌较多,一旦出现穿孔,与胃食管相比,出现腹膜炎的概率亦会增大,因此,其技术要求也相应有所提高。

Yahagi等<sup>[17-18]</sup>对146例结直肠局限于黏膜或有轻度黏膜下浸润的早期肿瘤病灶进行了ESD治疗,切除病灶直径平均为35.8 mm(6~109 mm),其中完整切除病灶者占92%(133例),另外13例虽然是分块切除,但病灶也均被完全切除。其中经病理证实有87%(127例)为R0切除。其中除了1例分块切除的病例出现了复发,其余病例在随访期内均未见复发。另有研究者对35例病变位于直肠的患者进行了ESD治疗,其临床整块切除及R0切除的病例分别占88.6%(31/35)和62.9%(22/35),术后患者血红蛋白下降均小于2 g/dl,有2例出现穿孔(5.7%),经内镜保守治疗好转<sup>[19]</sup>。上述临床资料表明,尽管对操作技术的要求有所提高,但ESD在治疗早期结直肠肿瘤方面,因其具有治愈率高、安全性好、可明显改善患者生活质量等优势,仍有着较好的应用前景。

## 4 十二指肠及近端空肠病变中的应用

ESD在十二指肠及近端空肠病变的治疗仅见少数个案报道,Yamazaki等去年在国际胃肠病学会会议上报告了2例十二指肠及近端空肠扁平腺瘤的ESD治疗,以评价其对十二指肠及近端空肠黏膜病变治疗的适应证,2例均得以成功切除,且经病理证实为腺瘤,为今后类似病例的治疗提供了借鉴。

## 5 小结

上述诸方面都证实了ESD在早期消化道肿瘤的治疗中起着举足轻重的地位,但对于浸润较深及伴有淋巴结转移的病例则不适合进行ESD治疗,因此早期发现肿瘤及术前对肿瘤进行准确的评估和分期是至关重要的。相信随着诊断及治疗技术的不断发展,早期消化道肿瘤的诊断和治疗会得到进一步的提高。

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(本文编辑:周骏)

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(收稿日期:2008-09-11)

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(收稿日期:2008-09-19)

(本文编辑:周骏)