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隧道法内镜下粘膜下剥离术治疗食道粘膜下肿瘤的临床价值 *

吴大鹏 孙仁虎△ 肖 君 金海林 李 杨

（南京中医药大学附属江苏省中医院消化内镜中心 江苏 南京 210029）

摘要 目的:探讨隧道法内镜下粘膜下剥离术治疗食道粘膜下肿瘤的临床价值。**方法:**2014 年 2 月至 2017 年 9 月选择在本院诊治的食道粘膜下肿瘤患者 172 例，根据手术方法的不同分为观察组 100 例与对照组 72 例。观察组给予隧道法内镜下粘膜下剥离术，对照组给予内镜粘膜下剥离术治疗，记录与随访两组的预后情况。**结果:**两组手术时间对比无差异(P>0.05)，观察组的术中出血量、术后禁食天数与术后住院时间显著少于(短于)对照组(P<0.05)。观察组术后 3 d 的并发症发生率为 3.0 %，显著低于对照组的 15.3 %(P<0.05)。观察组术后 1 d 与术后 14 d 的血清 IL-2、sIL-2R 含量都显著低于对照组(P<0.05)。随访 2 年，观察组的 1 年与 2 年复发率分别为 2.0 %和 6.0 %，显著低于对照组的 8.3 %和 15.3 %(P<0.05)。**结论:**隧道法内镜下粘膜下剥离术治疗食道粘膜下肿瘤能减少创伤，减少并发症的发生，降低复发率，并促进患者免疫功能的恢复。

关键词:隧道法内镜下粘膜下剥离术；食道粘膜下肿瘤；内镜粘膜下剥离术；免疫功能；复发

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Clinical Values of Endoscopic Submucosal Dissection under Tunneling for Treatment of Submucosal Tumors*

WU Da-peng, SUN Ren-hu△, XIAO Jun, JIN Hai-lin, LI Yang

(Department of Digestive Endoscopy, Jiangsu Provincial Hospital of Traditional Chinese Medicine, Nanjing University of Traditional Chinese Medicine, Nanjing, Jiangsu, 210029, China)

ABSTRACT Objective: To investigate the clinical value of Endoscopic submucosal dissection under tunneling in the treatment of Submucosal Tumors. **Methods:** From February 2014 to September 2017, 172 patients with Submucosal Tumors diagnosed and treated in our hospital were selected as subjects and were divided into the 100 patients in the observation group and 72 patients in the control group accorded to the different surgical methods. The observation group were given Endoscopic submucosal dissection under tunneling, and the control group were treated with Endoscopic Submucosal Dissection. The prognosis of the two groups were recorded and followed up. **Results:** There were no significant difference in the operation time compared between the two groups (P>0.05). The intraoperative blood loss, postoperative fasting days and postoperative hospital stay in the observation group were significantly less than in the control group (P<0.05). The postoperative 3 d of incidences were 3.0 % in the observation group, which were significantly lower than that in the control group of 15.3 %(P<0.05). The postoperative 1 d and 14 d levels of serum IL-2 and sIL-2R in the observation group were significantly lower than those in the control group(P<0.05). After 2 years of followed-up, the 1-year and 2-year recurrence rates of the observation group were 2.0 % and 6.0 %, respectively, which were significantly lower than the 8.3 % and 15.3 % of the control group(P<0.05). **Conclusion:** Endoscopic submucosal dissection with tunneling for the treatment of submucosal tumors of the esophagus can reduce trauma, reduce the incidence of complications, reduce the recurrence rate of patients, and promote the recovery of immune function.

Key words: Endoscopic submucosal dissection under tunneling; Submucosal Tumors; Endoscopic submucosal dissection; Immune function; Recurrence

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前言

食道是食物的运输管道，食道粘膜下肿瘤(Submucosal Tumors，SMTs)是指来自食道粘膜层以下以及食道管壁正常组织发生结构异常的肿瘤，包括平滑肌瘤、脂肪瘤、胃肠道间质瘤(Gastrointestinal Stromal Tumors，GISTs)等[1,2]。该病多为良性病变，约占所有食道肿瘤的不到 1 %，超过 95 %为良性病变，也有 5 %左右具有恶性潜能或为恶性病变[3,4]。该病的发病年龄一般在壮年，男性多于女性，在我国具有比较高的发病率[5]。食道粘膜下肿瘤的临床治疗方法包括手术、化疗、中医中药、放疗等，

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作者简介：吴大鹏(1985-)，男，硕士，主治医师，研究方向：消化道疾病内镜下诊治，电话：13770732243，E-mail：cindywu14@163.com

△ 通讯作者：孙仁虎(1980-)，男，博士，主治医师，研究方向：消化道疾病的内镜下诊治，电话：15951997297，E-mail: sunrehu1980@163.com

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其中手术为公认的根治方法，但是由于食道贯穿颈部胸部腹部,周围邻近的结构特殊,导致手术操作比较复杂,对于患者的创伤比较大,容易发生术后并发症,从而影响全身生理功能[6,7]。随着医学技术的发展，内镜治疗在临床上的应用越来越多,具有创伤小、术中出血量少、成功率高等优点[8]。其包括粘膜下肿瘤套扎术、内镜下粘膜切除术、内镜粘膜下剥离术、隧道法内镜下粘膜下剥离术等[9,10]。其中隧道法内镜下粘膜下剥离术是一种改良型 ESD 术，是在消化道固有肌层和黏膜层之间利用建立一条人工隧道,可剥离开粘膜层与固有肌层,且利用隧道对食道各层病变进行操作,使两层组织形成双重屏障,能缩小了创面及降低内镜下操作难度和风险[11,12]。本文具体探讨了隧道法内镜下粘膜下剥离术治疗食道粘膜下肿瘤的临床价值,现报告如下。

1 资料与方法

1.1 研究对象

2014 年 2 月至 2017 年 9 月选择在本院诊治的食道粘膜下肿瘤患者 172 例,纳入标准:术前影像学诊断为食道粘膜下肿瘤,术前普通胃镜及超声胃镜确诊为食道粘膜下肿瘤;无精神疾病,自愿参加者;本院伦理委员会批准了此次研究;患者既往未行内镜下微创手术、化疗及放疗等任何治疗；年龄 30-75 岁,具有手术治疗适应征;临床与调查资料完整。排除标准:精神障碍、哺乳期及妊娠期患者;病变处可见食道静脉曲张者;凝血系统功能异常未达到手术要求者；病变处可见食道憩室者;神经系统器质性疾病患者。

根据手术方法的不同分为观察组 100 例与对照组 72 例,两组患者的肿瘤直径、性别、年龄、体重指数、临床分期、发病位置等对比差异无统计学意义(P>0.05)。见表 1。

表 1 一般资料对比

Table 1 Comparison of general data

Groups	n	Gender (Male/ Female)	Old (years)	BMI (kg/m^2)	Incidence location (upper/middle/lower)	Tumor diameter (cm)
Observation group	100	56/44	58.82± 4.45	22.42± 1.48	30/40/30	1.78± 0.31
Control group	72	38/34	58.20± 4.35	22.10± 2.41	22/30/20	1.80± 0.22

1.2 治疗方法

所有患者术前禁食禁水时间 12 h,整个操作在气管插管全麻下进行,全程使用二氧化碳充气。使用奥林巴斯的 GIF Q260 内镜,配有 IT 刀、钩刀、电凝钳、透明帽、钛夹等。

观察组:给予隧道法内镜下粘膜下剥离术,患者取左侧卧位,麻醉后将食道内残留物冲洗清除,明确病变部位。安装透明帽于内镜前端，于病灶上方 2-3 cm 处距病灶黏膜下注射亚甲蓝 +0.9 %氯化钠溶液后横向切开粘膜,将近端黏膜处分离出来隧道,沿隧道向下分离至病灶处,游离病灶四周粘膜层及肌层并进行切断,直至完整剥离。对粘膜下层暴露出的小血管进行充分电凝止血处理,使用钛夹逐步关闭粘膜缺口。

对照组:给予内镜粘膜下剥离术治疗,切开病灶周围黏膜,然后剥离病灶,肿瘤物完全剥离后止血,用钛夹处理窗口,冲洗创面。

所有患者术后卧床休息 1-3 d,嘱禁食、抑制胃酸、补液、预防性使用止血药物和抗菌药物。

1.3 观察指标

(1)术中出血量、手术时间、术后禁食天数与术后住院时间。(2)术后 3 d 出现的出血、气胸、穿孔、皮下气肿等并发症发生情况。(3) 在术后 1 d 与术后 14 d 采用酶联免疫测定血清白介素(白介素,IL)-2 和可溶性白介素 -2 受体(Soluble interleukin-2 receptor,sIL-2R)含量。(4)所有患者随访 2 年,记录患者的 1 年与 2 年复发率情况。

1.4 统计方法

采用 SPSS22.00,计量数据选择均数± 标准差表示,并发症发生率计数数据(%)表示,行 t 检验与 x^2 分析,P<0.05 有统计学意义。

2 结果

2.1 围手术指标对比

两组手术时间无差异(P>0.05),观察组的术中出血量、术后禁食天数与术后住院时间显著少于(短于)对照组(P<0.05)。见表 2。

表 2 围手术指标对比 ($\bar{x}$± s)

Table 2 Comparison of perioperative indicators ($\bar{x}$± s)

Groups	n	Operation time (min)	Intraoperative bleeding volume (mL)	Days of fasting after operation (d)	Postoperative hospital stay (d)
Observation group	100	44.95± 15.43	24.42± 10.13*	1.78± 0.443*	6.48± 1.113*
Control group	72	42.09± 15.42	45.58± 12.24	3.14± 0.32	9.00± 0.87

Note: compare with the control group, *P<0.05.

2.2 并发症情况对比

观察组术后 3 d 的出血、气胸、穿孔、皮下气肿发生率显著低于对照组(P<0.05)。见表 3。

表 3 并发症发生情况对比(例,%)

Table 3 Comparison of postoperative complications (n,%)

Groups	n	Haemorrhage	Aerothorax	Perforation	Aerodermectasia	Total
Observation group	100	1	1	0	1	3 (3.0)*
Control group	72	2	3	2	4	11 (15.3)

2.3 炎症因子表达对比

观察组术后 1 d 与术后 14 d 的血清 IL-2、sIL-2R 含量都显著低于对照组(P<0.05)。见表 4。

表 4 血清炎症因子表达对比($\bar{x}\pm s$)

Table 4 Comparison of serum inflammatory factors expression ($\bar{x}\pm s$)

Groups	n	IL-2 (pg/mL)		sIL-2R (U/mL)	
		Postoperative 1 d	Postoperative 14 d	Postoperative1 d	Postoperative 14 d
Observation group	100	8.98± 1.15*	1.84± 0.53*	378.40± 44.20*	50.23± 8.62*
Control group	72	13.33± 1.45	4.45± 0.56	709.39± 50.39	117.40± 19.14

2.4 复发率对比

随访 2 年,观察组的 1 年与 2 年复发率分别为 2.0 %和 6.0 %,显著低于对照组的 8.3 %和 15.3 % (P<0.05)。见表 5。

表 5 随访复发率对比(例,%)

Table 5 Comparison of recurrence rates (n,%)

Groups	n	1 year recurrence rate	2 year recurrence rate
Observation group	100	2 (2.0)*	6 (6.0)*
Control group	72	6 (8.3)	11 (15.3)

3 讨论

随着消化道内镜检查的增多与其他改进诊断方式的使用,当前食道粘膜下肿瘤的发病人数逐年增加, 主要包括平滑肌瘤、间质瘤、脂肪瘤、类癌、纤维瘤等[13,14]。该病在临床上缺乏特异性的体征、症状和实验室指标,多数情况下是由患者接受内镜检查意外发现[15]。手术为该病的主要治疗方法,手术完整切除率都在 95 %以上。不过传统外科手术存在创伤大、恢复慢以及危险性高等缺点[16,17]。比如内镜下粘膜剥离术已逐渐替代传统手术治疗食道粘膜下肿瘤,其在切除病变时要求相对低。但是由于食道管腔狭小,内镜剥离过程中粘膜组织易堆积于管腔中,导致手术难度增高、风险比较大[18]。隧道法内镜下粘膜下剥离术为通过内镜在食道黏膜下建立的一条位于黏膜层与固有肌层之间隧道,可使得手术操作更加快速、安全与简单,并可保持食道完整性。特别是该方法能更快速、完整切除病变,手术视野清晰,可以充分暴露血管,从而方便手术操作[19,20]。本研究显示两组手术时间无差异,观察组的术中出血量、术后禁食天数与术后住院时间减少,表明隧道法内镜下粘膜下剥离术治疗食道粘膜下肿瘤能减少手术创伤,促进患者康复。

内镜治疗是指通过麻醉剂,使患者在无知觉的情况下完成诊治。内镜手术一直被视为治疗食道粘膜下肿瘤的标准方法,但是也有可能并发穿孔等并发症,并且存在定位差、愈合时间长等缺点,严重时需要外科处理[21,22]。隧道法内镜下粘膜下剥离术最初仅用于固有肌层的肿瘤,遵循了暴露与直视充分的手术原则,在保证操作安全性与治疗效果的基础上,可减少损伤较大血管及固有肌层的风险[23]。本研究显示观察组术后 3 d 的出血、气胸、穿孔、皮下气肿等并发症发生率为 3.0 %,显著低于对照组的 15.3 %。为减少并发症发生,在分离黏膜下层时应时刻注意止血,避免视野模糊引起食道穿孔,尽量保证一次性止血成功。在剥离肿瘤时,要以肌筋膜为参照,垂直环形肌方向进行剥离,防止隧道偏向,掌握剥离的深浅层次,从而保持固有肌层完整性,有利于减少术后并发症的发生[24]。

食道粘膜下肿瘤的处理方式取决于患者的临床症状与病灶情况,手术切除是该病的主要治疗方法,手术方式包括开胸手术和内镜下切除治疗。内镜治疗具有术中出血量少、创伤小、成功率高等特点,有利于患者早期术后康复。免疫功能对于肿瘤患者的术后恢复及预后甚为重要,而食道粘膜下肿瘤、内镜手术、麻醉及疼痛等因素可进一步显著抑制患者的免疫功能,并导致机体强烈的应激反应,不利于术后患者的康复[25]。IL-2 在肿瘤的细胞免疫中发挥十分重要的作用,其血清水平的高低可反映机体的免疫状态[26]。其可以与 sIL-2R 形成动态免疫调节网络,维持机体正常的免疫调节功能[27]。本研究显示观察组术后 1 d 与术后 14 d 的血清 IL-2、sIL-2R 含量都显著低于对照组,说明隧道法内镜下粘膜下剥离术治疗食道粘膜下肿瘤能更加有效促进患者免疫功能的恢复。有研究显示采用多隧道剥离食道黏膜病变时,可以通过借助周边黏膜的牵引力,保留隧道病变两侧黏膜,可获得清晰的隧道操作空间,从而减少对患者免疫功能的负面影响[28]。

隧道法内镜下粘膜下剥离术可建立粘膜下隧道并分离粘膜下层，可边注射液体边剥离，缩短剥离时间，减少手术创伤[29,30]。本研究显示随访2年，观察组的1年与2年复发率分别为2.0 %和6.0 %，显著低于对照组的8.3 %和15.3 %，说明隧道法内镜下粘膜下剥离术在病灶剥离的完整性上具有明显优势。不过本研究存在一定的不足，隧道法内镜下粘膜下剥离术的机制分析还不够深入，随访的时间较短，且病例数较少，将在后续研究中进行探讨。

总之，隧道法内镜下粘膜下剥离术治疗食道粘膜下肿瘤能减少创伤和并发症的发生，降低复发率，促进免疫功能的恢复。

参 考 文 献(References)

[1] Chai N, Du C, Gao Y, et al. Correction to: Comparison between submucosal tunneling endoscopic resection and video-assisted thoracoscopic enucleation for esophageal submucosal tumors originating from the muscularis propria layer: a randomized controlled trial[J]. Surg Endosc, 2018, 32(7): e3373

[2] Chai N, Zhang W, Linghu EQ. Prepyloric submucosal tunneling endoscopic resection for a case of inflammatory mass (with video)[J]. Dig Endosc, 2018, 30(4): 546-547

[3] Chen H, Li B, Li L, et al. Current Status of Endoscopic Resection of Gastric Subepithelial Tumors [J]. Am J Gastroenterol, 2019, 114(5): 718-725

[4] Chiu P WY, Yip HC, Teoh A YB, et al. Per oral endoscopic tumor (POET) resection for treatment of upper gastrointestinal subepithelial tumors[J]. Surg Endosc, 2019, 33(4): 1326-1333

[5] Du C, Chai N, Linghu E, et al. Treatment of cardial submucosal tumors originating from the muscularis propria layer: submucosal tunneling endoscopic resection versus endoscopic submucosal excavation[J]. Surg Endosc, 2018, 32(11): 4543-4551

[6] Du C, Chai NL, Ling-Hu EQ, et al. Submucosal tunneling endoscopic resection: An effective and safe therapy for upper gastrointestinal submucosal tumors originating from the muscularis propria layer[J]. World J Gastroenterol, 2019, 25(2): 245-257

[7] Ingason AB, Theodors A, Agustsson AS, et al. Giant gastric lipoma successfully removed by endoscopic submucosal dissection: case report and systematic review [J]. Scand J Gastroenterol, 2018, 53(8): 1018-1024

[8] Marcella C, Shi R, Yu T, et al. Asymptomatic esophageal glomus tumor: case report[J]. J Gastrointest Oncol, 2019, 10(5): 1015-1020

[9] Mavrogenis G, Bazerbachi F, Tsevgas I, et al. Endoscopic submucosal dissection and submucosal tunneling endoscopic resection for obstructive lipomas of the foregut and hindgut[J]. VideoGIE, 2019, 4(5): 226-229

[10] Peng L, Zhou P, Zhang G. Submucosal tunneling endoscopic resection of a gigantic cardiac leiomyoma [J]. Dig Endosc, 2018, 30(5): 694-696

[11] Peng W, Tan S, Huang S, et al. Efficacy and safety of submucosal tunneling endoscopic resection for upper gastrointestinal submucosal tumors with more than 1-year' follow-up: a systematic review and meta-analysis[J]. Scand J Gastroenterol, 2019, 54(4): 397-406

[12] Peng W, Tang X, Fu X. Submucosal tunneling endoscopic resection of a large esophageal leiomyoma using endoscopy with near-focus mode[J]. Dig Endosc, 2018, 30(5): e680

[13] Song S, Feng M, Zhou H, et al. Submucosal Tunneling Endoscopic Resection for Large and Irregular Submucosal Tumors Originating from Muscularis Propria Layer in Upper Gastrointestinal Tract [J]. J Laparoendosc Adv Surg Tech A, 2018, 28(11): 1364-1370

[14] Song S, Wang X, Zhang S, et al. Efficacy and complications of submucosal tunneling endoscopic resection for upper gastrointestinal submucosal tumors and exploration for influencing factors[J]. Z Gastroenterol, 2018, 56(4): 365-373

[15] Wang Z, Zhang J, Mi J, et al. Expression and significance of interleukin-17 and interleukin-22 in the serum and the lower esophageal sphincter of patients with achalasia [J]. Saudi J Gastroenterol, 2018, 24(4): 242-248

[16] Wang Z, Zheng Z, Wang T, et al. Submucosal tunneling endoscopic resection of large submucosal tumors originating from the muscularis propria layer in the esophagus and gastric cardia [J]. Z Gastroenterol, 2019, 57(8): 952-959

[17] Xiong Y, Chen QQ, Chai NL, et al. Endoscopic trans-esophageal submucosal tunneling surgery: A new therapeutic approach for diseases located around the aorta ventralis[J]. World J Gastroenterol, 2019, 25(1): 85-94

[18] Suzuki T, Kitagawa Y, Nankinzan R, et al. Feasibility of endoscopic submucosal dissection for recurrent colorectal tumors after endoscopic mucosal resection[J]. Acta Gastroenterol Belg, 2019, 82(3): 375-378

[19] Zhang SL, Du X, Tang XY, et al. Submucosal tunneling endoscopic resection for an unusually sized esophageal submucosal tumor protruding into the mediastinum [J]. Rev Esp Enferm Dig, 2019, 111(9): 710-711

[20] Chen W, Zhu XN, Wang J, et al. Risk factors for Mallory-Weiss Tear during endoscopic submucosal dissection of superficial esophageal neoplasms[J]. World J Gastroenterol, 2019, 25(34): 5174-5184

[21] Figueiroa G, Pimentel-Nunes P, Dinis-Ribeiro M, et al. Gastric endoscopic submucosal dissection: a systematic review and meta-analysis on risk factors for poor short-term outcomes [J]. Eur J Gastroenterol Hepatol, 2019, 31(10): 1234-1246

[22] Gaiani F, De'angelis N, Minelli R, et al. Pediatric gastroenteropancreatic neuroendocrine tumor: A case report and review of the literature [J]. Medicine (Baltimore), 2019, 98(37): e17154

[23] Hirata D, Kashida H, Iwatate M, et al. Effective use of the Japan Narrow Band Imaging Expert Team classification based on diagnostic performance and confidence level [J]. World J Clin Cases, 2019, 7(18): 2658-2665

[24] Hwang Y, Yoon YS, Bong JW, et al. Long-term Transanal Excision Outcomes in Patients With T1 Rectal Cancer: Comparative Analysis of Radical Resection[J]. Ann Coloproctol, 2019, 35(4): 194-201

[25] Jin XF, Gai W, Du RL, et al. Multiband mucosectomy versus endoscopic submucosal dissection and endoscopic submucosal excavation for GI submucosal tumors: short and long term follow-up[J]. BMC Cancer, 2019, 19(1): 893-901

[26] Kim HG, Park MS, Sung JY, et al. Tumor-specific Expression of Insulin-like Growth Factor II mRNA-binding Protein 3 Independently Predicts Worse Survival of Patients With Adenocarcinoma of the Ampulla of Vater[J]. Anticancer Res, 2019, 39(9): 4947-4955

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参 考 文 献(References)

[1] Zheng J, Feng Z, Zhu J. Effect of preintravenous injection of parecoxib, combined with transversus abdominis plane block in strategy of enhanced recovery after radical resection of colorectal cancer [J]. J Cancer Res Ther, 2018, 14(7): 1583-1588

[2] Cai X, Gu D, Chen M, et al. The effect of the primary tumor location on the survival of colorectal cancer patients after radical surgery[J]. Int J Med Sci, 2018, 15(14): 1640-1647

[3] 王珏, 张婷婷, 李娟, 等. 不同原发肿瘤位置对于西妥昔单抗联合化疗治疗 K-ras 基因野生型的转移性结直肠癌患者的预后比较[J]. 现代生物医学进展, 2016, 16(6): 1153-1155, 1123

[4] Matsuyama T, Kinugasa Y, Nakajima Y, et al. Robotic-Assisted Surgery - Current State of the Art and Future Perspective Colorectal Cancer[J]. Gan To Kagaku Ryoho, 2018, 45(12): 1696-1700

[5] Law E, Levesque JV, Lambert S, et al. The "sphere of care": A qualitative study of colorectal cancer patient and caregiver experiences of support within the cancer treatment setting [J]. PLoS One, 2018, 13 (12): e0209436

[6] Huang Z, Yang M, Li Y, et al. Exosomes Derived from Hypoxic Colorectal Cancer Cells Transfer Wnt4 to Normoxic Cells to Elicit a Prometastatic Phenotype[J]. Int J Biol Sci, 2018, 14(14): 2094-2102

[7] Flemer B, Lynch DB, Brown JMR, et al. Tumour-associated and non-tumour-associated microbiota in colorectal cancer[J]. Gut, 2017, 66(4): 633-643

[8] Gao Y, Wang J, Zhou Y, et al. Evaluation of Serum CEA,CA19-9, CA72-4, CA125 and Ferritin as Diagnostic Markers and Factors of Clinical Parameters for Colorectal Cancer [J]. Sci Rep, 2018, 8(1): 2732

[9] Mariampillai AI, Cruz JPD, Suh J, et al. Cancer Antigen 72-4 for the Monitoring of Advanced Tumors of the Gastrointestinal Tract, Lung, Breast and Ovaries[J]. Anticancer Res, 2017, 37(7): 3649-3656

[10] Yang W, Luo Y, Hu S, et al. Value of combined detection of serum carcino-embryonic antigen, carbohydrate antigen 19-9 and cyclooxygenase-2 in the diagnosis of?colorectal cancer [J]. Oncol Lett, 2018, 16(2): 1551-1556

[11] Cai J, Ma H, Huang F, et al. Low expression of RSK4 predicts poor prognosis in patients with colorectal cancer [J]. Int J Clin Exp Pathol, 2014, 7(8): 4959-4970

[12] Tan HY, Zheng YB, Liu J. Serum miR-199a as a potential diagnostic biomarker for detection of colorectal cancer[J]. Eur Rev Med Pharmacol Sci, 2018, 22(24): 8657-8663

[13] 李道娟, 李倩, 贺宇彤. 结直肠癌流行病学趋势[J].肿瘤防治研究, 2015, 42(3): 305-310

[14] Khoja A, Aljawadi M, Al-Shammari SA, et al. Utilization of Colorectal Cancer Screening among Saudi Elderly Population: A Study from the Saudi National Survey for Elderly Health [J]. Asian Pac J Cancer Prev, 2018, 19(12): 3401-3407

[15] Liang Y, Zhang C, Ma MH, et al. Identification and prediction of novel non-coding and coding RNA-associated competing endogenous RNA networks in colorectal cancer [J]. World J Gastroenterol, 2018, 24(46): 5259-5270

[16] Abbaszadegan MR, Moghbeli M. Genetic and molecular origins of colorectal Cancer among the Iranians: an update [J]. Diagn Pathol, 2018, 13(1): 97

[17] 易呈浩, 葛维挺, 黄彦钦, 等. 1368 例结直肠癌 TNM 分期及预后分析[J].中国肿瘤临床, 2012, 39(9): 597-601

[18] Rees CJ, Rajasekhar PT, Wilson A, et al. Narrow band imaging optical diagnosis of small colorectal polyps in routine clinical practice: the Detect Inspect Characterise Resect and Discard 2 (DISCARD 2) study[J]. Gut, 2017, 66(5): 887-895

[19] 杨刚, 唐丽娟. 血清 TuM 2-PK、CEA 、CA19-9 和 CA72-4 对结肠癌的筛查价值[J].检验医学与临床, 2017, 14(1): 35-36, 39

[20] Lech G, Słotwiński R, Słodkowski M, et al. Colorectal cancer tumour markers and biomarkers: Recent therapeutic advances [J]. World J Gastroenterol, 2016, 22(5): 1745-1755

[21] Vacante M, Borzì AM, Basile F, et al. Biomarkers in colorectal cancer:Current clinical utility and future perspectives [J]. World J Clin Cases, 2018, 6(15): 869-881

[22] Ning S, Wei W, Li J, et al. Clinical significance and diagnostic capacity of serum TK1, CEA, CA 19-9 and CA 72-4 levels in gastric and colorectal cancer patients[J]. J Cancer, 2018, 9(3): 494-501

[23] 唐承璐, 刘慧敏, 吕小红, 等. 血清 YKL-40、CEA、CA72-4 联合检测对结肠癌的诊断价值[J].中国实验诊断学, 2015, 19(4): 645-646

[24] 王科学. 血清 CEA、CA199、CA242 及 CA724 联合检测对结直肠癌诊断的临床价值[J].中国医师杂志, 2016, 18(3): 422-424

[25] Lei XF, Jia SZ, Ye J, et al. Application values of detection of serum CA199, CA242 and CA50 in the diagnosis of pancreatic cancer [J]. J Biol Regul Homeost Agents, 2017, 31(2): 383-388

[26] 韩晓颖, 王劲松, 李小芬, 等. 血清 CRP、CA72-4 水平变化与结直肠癌发生发展的关系[J].癌症进展, 2017, 15(6): 657-659

[27] 李娜, 李宏斌, 朱蕾, 等. 血清 CEA、CA199 和 CA153 检测对判定结肠癌发生发展的价值分析 [J]. 实用癌症杂志, 2016, 31(3): 396-398

[28] 杨姣, 陈贝贝, 吕慧芳, 等. 结直肠癌 K-ras 基因、血清 CEA 和 CA199 与临床病理的相关性 [J]. 现代肿瘤医学, 2015, 23(11): 1553-1556

[29] Wang C, Yu J, Han Y, et al. Long non-coding RNAs LOC285194, RP11-462C24.1 and Nbla12061 in serum provide a new approach for distinguishing patients with colorectal cancer from healthy controls [J]. Oncotarget, 2016, 7(43): 70769-70778

[30] Zhou B, Guo R. Genomic and regulatory characteristics of significant transcription factors in colorectal cancermetastasis [J]. Sci Rep, 2018, 8(1): 17836

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[27] Lee BE. Potential for Peritoneal Metastasis after Gastric Perforation Induced by Endoscopic Submucosal Dissection of Early Gastric Cancer[J]. Gut Liver, 2019, 13(5): 481-482

[28] Liu B, Chen H, Zhang W, et al. A novel technique for removing large gastric subepithelial tumors with ESD method in the subcardia region [J]. Oncol Lett, 2019, 18(5): 5277-5282

[29] Lu JX, Liu DL, Tan YY. Clinical outcomes of endoscopic submucosal tunnel dissection compared with conventional endoscopic submucosal dissection for superficial esophageal cancer: a systematic review and meta-analysis[J]. J Gastrointest Oncol, 2019, 10(5): 935-943

[30] Eba S, Notsuda H, Hoshi F, et al. Successful Multidisciplinary Treatment Accomplished by Collaboration of Multiple Clinical Departments for Synchronous Quadruple Cancer [J]. Kyobu Geka, 2019, 72 (9): 655-657