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论著

早期食管癌和高级别上皮内瘤变行内镜黏膜下剥离术后非治愈性切除的危险因素探讨

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摘要: **目的** 探讨早期食管癌和高级别上皮内瘤变行内镜黏膜下剥离术(ESD)后非治愈性切除的危险因素。**方法** 回顾性分析南京医科大学附属淮安第一医院消化内科收治的153例行ESD的早期食管癌和高级别上皮内瘤变患者的临床资料,根据术后病理结果,分为治愈性切除组和非治愈性切除组,对可能影响非治愈性切除的相关因素进行多因素分析。**结果** 早期食管癌、病变黏膜下浸润和术中抬举征欠佳为早期食管癌和高级别上皮内瘤变行ESD后非治愈性切除的危险因素($P < 0.05$)。多因素分析显示,病变为早期食管癌、存在黏膜下浸润为早期食管癌和高级别上皮内瘤变行ESD后非治愈性切除的独立危险因素($P < 0.05$)。**结论** 早期食管癌、病变黏膜下浸润、术中抬举征欠佳为早期食管癌和高级别上皮内瘤变行ESD后非治愈性切除的危险因素,其中早期食管癌和存在黏膜下浸润为非治愈性切除的独立危险因素。

关键词: 内镜黏膜下剥离术;非治愈性切除;早期食管癌;高级别上皮内瘤变;危险因素

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Discussion of risk factors for non-curative resection after endoscopic submucosal dissection for early esophageal cancer and high-grade intraepithelial neoplasia

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Abstract: Objective To investigate the possible risk factors for non-curative resection after endoscopic submucosal dissection for early esophageal cancer and high-grade intraepithelial neoplasia. **Methods** The clinical data of 153 patients with early esophageal cancer and high-grade intraepithelial neoplasia treated by endoscopic submucosal dissection were retrospectively analyzed. According to the postoperative pathological results, they were divided into the curative resection group and non-curative resection group, and a multivariate analysis was performed to determine the factors that might influence noncurative resection. **Results** Early esophageal cancer, submucosal infiltration of the lesion, and poor intraoperative lesion lift were risk factors for non-curative resection after ESD for early esophageal cancer and high-grade intraepithelial neoplasia ($P < 0.05$). Multivariate analysis showed that the lesions were early esophageal cancer, the existence of submucosal infiltration was the independent risk factors for non-curative resection after ESD for early esophageal cancer and high-grade intraepithelial neoplasia

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($P < 0.05$). **Conclusion** Early esophageal cancer, submucosal invasion of the lesion, and poor intraoperative lesion lift are risk factors for non-curative resection after early esophageal cancer and high-grade intraepithelial neoplasia. Among them, early esophageal cancer and the presence of submucosal infiltration were independent risk factors for non-curative resection.

Keywords: endoscopic submucosal dissection; non-curative resection; early esophageal cancer; high-grade intraepithelial neoplasia; risk factor

食管癌是一种侵袭性高、致死性强的恶性肿瘤,居全球第8位,每年死亡人数超过40万,在癌症相关死亡原因中排第6位,其5年生存率为15%~25%^[1-2]。早期食管癌患者一般无症状,横断面成像技术很少能发现病变,即使是内镜检查,可见的异常往往也不显著^[3]。食管高级别上皮内瘤变为食管癌的癌前病变,一项随访研究^[2]显示,74%的食管高级别上皮内瘤变患者会发展为食管癌。欧洲胃肠道内镜学会临床指南^[4]提示,食管高级别上皮内瘤变是内镜黏膜下剥离术(endoscopic submucosal dissection, ESD)的绝对适应证。随着内镜检查的普及和内镜诊断技术的发展,越来越多的早期食管鳞状细胞癌被发现,因内镜下黏膜切除术(endoscopic mucosal resection, EMR)具有侵袭性较小和治疗效果较好的优势,已成为早期食管癌的首选治疗方法,但ESD的整体切除率较EMR更高,局部复发率更低^[5-6]。有文献^[7]报道,ESD可有效根除不典型增生和早期癌症。虽然ESD治疗效果良好,但可能发生非治愈性切除。本文主要探讨早期食管癌和高级别上皮内瘤变患者行ESD后发生非治愈性切除的危险因素。

1 资料与方法

1.1 一般资料

回顾性分析2015年4月—2020年4月南京医科大学附属淮安第一医院消化科收治的153例行ESD的早期食管癌和高级别上皮内瘤变患者的临床资料,根据术后病理结果,分为治愈性切除组和非治愈性切除组。其中,治愈性切除组122例,非治愈性切除组31例。治愈性切除指:整块切除、无脉管浸润、黏膜下浸润深度 $< 200 \mu\text{m}$ 、水平及基底切缘均为阴性、组

织学类型为高或中分化。不满足治愈性切除标准者为非治愈性切除^[8]。

153例接受ESD治疗的早期食管癌和高级别上皮内瘤变患者中,男98例,女55例,年龄(62.4 ± 7.8)岁,早期食管癌39例(25.5%),高级别上皮内瘤变114例(74.5%)。早期食管癌非治愈性切除15例(38.5%),高级别上皮内瘤变非治愈性切除16例(14.0%),病变整块切除143例(93.5%),病变完全切除127例(83.0%)。

纳入标准:术前诊断为早期食管癌或高级别上皮内瘤变者;术后病理诊断为早期食管癌或高级别上皮内瘤变者;病变局限在上皮层或黏膜固有层、浸润黏膜肌层或黏膜下浅层但无淋巴结转移者(超声或胸部CT检查均未见异常淋巴结)。排除标准:病变浸润至黏膜下深层者;发生淋巴结转移者;内镜手术未顺利完成者。

1.2 方法

操作均由同一内镜医生(具备5年内镜操作经验)完成,所有患者均于全身麻醉下行ESD,采用碘染色及氩气对病灶周围进行标记后,黏膜下注射使病灶抬举,再环周切开黏膜,行黏膜下病灶剥离,切除病灶,最后处理创面。切除的病变标本立即置于福尔马林中固定24 h,每隔2 mm连续垂直切片,行病理学检查。比较非治愈性切除组与治愈性切除组患者的临床资料,以寻找可能导致非治愈性切除的危险因素。

1.3 统计学方法

选用SPSS 22.0软件进行统计分析,计数资料以例表示,行 χ^2 检验;采用二元Logistic回归分析行多因素分析。 $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 影响非治愈性切除的单因素分析

将两组患者的临床资料进行单因素分析，结果显示：非治愈性切除患者的性别、年龄、是否合并高血压及糖尿病、有无消化道肿瘤家族史、病变部位、内镜下分型和治愈性切除比较，差异无统计学意义 ($P >$

0.05)；早期食管癌、病变黏膜下浸润和术中抬举征欠佳为非治愈性切除的危险因素 ($P < 0.05$)。见表 1。

2.2 影响非治愈性切除的多因素分析

将单因素分析得到显著差异的指标（术后病理类型、有无黏膜下浸润和术中抬举征）纳入多因素分析，结果显示：早期食管癌和存在黏膜下浸润为非治愈性切除的独立危险因素。见表 2。

表 1 影响非治愈性切除的单因素分析 例

Table 1 Univariate analysis of influencing factors of non-curative resection n

组别	性别		年龄		高血压		糖尿病		消化道肿瘤家族史		术后病理	
	男	女	≤65岁	>65岁	有	无	有	无	有	无	早期食管癌	高级别上皮内瘤变
非治愈性切除组 (n = 31)	18	13	20	11	10	21	3	28	6	25	15	16
治愈性切除组 (n = 122)	80	42	76	46	37	85	9	113	16	106	24	98
χ ² 值	0.61		0.05		0.04		0.18		0.78		10.73	
P值	0.437		0.819		0.835		0.710		0.377		0.001	

组别	病变部位			内镜下分型			黏膜下浸润		术中抬举征	
	上 1/3	中 1/3	下 1/3	隆起型病变	平坦型病变	凹陷型病变	有	无	良好	欠佳
非治愈性切除组 (n = 31)	5	14	12	9	20	2	8	23	26	5
治愈性切除组 (n = 122)	10	71	41	25	94	3	5	117	118	4
χ ² 值	2.53			2.54			14.98		7.37	
P值	0.259			0.281			0.001		0.007	

表 2 影响非治愈性切除的多因素分析

Table 2 Multivariate analysis of influencing factors of non-curative resection

因素	B	SE	Walds	OR	95%CI	P值
术后病理	-1.218	0.451	7.309	0.296	0.122 ~ 0.715	0.007
黏膜下浸润	-1.814	0.738	6.041	0.163	0.038 ~ 0.692	0.014
术中抬举征	0.369	0.932	0.156	1.446	0.233 ~ 8.981	0.692

3 讨论

内镜下微创手术是早期食管癌和高级别上皮内瘤变的首选治疗方案，包括EMR和ESD，与开放手术相比，可以明显缩短住院时间、减少并发症发生，并改善患者术后生活质量^[9-10]，是非侵入性、价格适中的治疗方法，但仅限于黏膜层且无淋巴结转移的病变，患者的中位无瘤生存率与开放手术治疗相似^[11]。

EMR的整块切除仅限于较小的病灶，且常行零碎切除，切除后无法通过组织学确认是否完全切除，常导致复发；ESD的整块切除对病灶大小没有限制，可以提高完全切除的组织病理学评估精确度，并降低复发的风险^[12]。ISOMOTO等^[13]报道，早期食管癌行ESD治疗，鳞状细胞癌的整块切除率为90%~100%、治愈性切除率为88%~99.1%，腺癌的整块切除率为97%~100%、治愈性切除率为79%~97%。

PROBST等^[12]报道,食管早期原发性腺癌的整体切除率为95.4%、完全切除率为83.9%、治愈率为72.4%,而早期鳞状细胞癌的整体切除率为100.0%、完全切除率为91.7%、治愈率为45.8%。国内文献^[8]报道,ESD治疗的整块切除率为80%~100%,完全切除率为74%~100%。

早期食管癌和癌前病变行ESD的绝对适应证为食管黏膜重度异型增生,病变局限在上皮层或黏膜固有层;相对适应证为病变浸润至黏膜肌层或黏膜下浅层但无淋巴结转移;禁忌证为发现有淋巴结转移的病变,术前判断病变浸润至黏膜下深层;相对禁忌证为非抬举征阳性,虽然病变浸润至黏膜下深层,但患者不能或不愿行外科手术。本研究发现,病变存在黏膜下浸润和术中抬举征欠佳的患者易发生非治愈性切除。其中,黏膜下浸润为非治愈性切除的独立危险因素。因此,非绝对适应证的存在会增加非治愈性切除的风险,在临床工作中对于不符合ESD绝对适应证的患者,需详尽地了解病变情况,并格外注意术中操作,以避免非治愈性切除的发生^[14]。此外,术者本身的水平及经验对患者能否得到治愈性切除也存在一定影响。有研究^[15]显示,肿瘤尺寸较大、术中抬举征欠佳和手术时间较长与非治愈性切除相关。一项关于早期胃癌行ESD的研究^[16]显示,技术欠佳、病变较大、手术时间长、术前误诊和经验不足的内镜医师与非治愈性切除明显相关,非治愈性切除主要原因是技术不足和术前误诊。

综上所述,早期食管癌、病变黏膜下浸润和术中抬举征欠佳为早期食管癌和高级别上皮内瘤变行ESD后非治愈性切除的危险因素。其中,早期食管癌和存在黏膜下浸润为非治愈性切除的独立危险因素。但本研究为回顾性分析,且纳入病例数较少,仍需进一步扩大样本量来证实。

参 考 文 献 :

- [1] TALUKDAR F R, DI PIETRO M, SECRIER M, et al. Molecular landscape of esophageal cancer: implications for early detection and personalized therapy[J]. *Ann N Y Acad Sci*, 2018, 1434(1): 342-359.
- [2] SANG H M, CAO J L, SOYFOO M D, et al. Endoscopic and histopathology characteristics in patients with esophageal high-grade intraepithelial neoplasia[J]. *Dig Surg*, 2019, 36(5): 384-393.
- [3] SPATARO J, ZFASS A M, SCHUBERT M, et al. Early esophageal cancer: a gastroenterologist's disease[J]. *Dig Dis Sci*, 2019, 64(11): 3048-3058.
- [4] PIMENTEL-NUNES P, DINIS-RIBEIRO M, PONCHON T, et al. Endoscopic submucosal dissection: European Society of Gastrointestinal Endoscopy (ESGE) guideline[J]. *Endoscopy*, 2015, 47(9): 829-854.
- [5] SHIMIZU Y, KATO M, YAMAMOTO J, et al. Histologic results of EMR for esophageal lesions diagnosed as high-grade intraepithelial squamous neoplasia by endoscopic biopsy[J]. *Gastrointest Endosc*, 2006, 63(1): 16-21.
- [6] KIM J A, SHAH P M. Screening and prevention strategies and endoscopic management of early esophageal cancer[J]. *Chin Clin Oncol*, 2017, 6(5): 50.
- [7] UNO K, KOIKE T, KUSAKA G, et al. Risk of metachronous recurrence after endoscopic submucosal dissection of esophageal squamous cell carcinoma[J]. *Dis Esophagus*, 2017, 30(6): 1-8.
- [8] 国家卫生健康委员会. 食管癌诊疗规范(2018年版)[J]. *中华消化病与影像杂志: 电子版*, 2019, 9(4): 158-192.
- [8] National Health Commission. Guidelines for the diagnosis and treatment of esophageal cancer (2018 edition)[J]. *Chinese Journal of Digestion and Medical Imageology: Electronic Edition*, 2019, 9(4): 158-192. Chinese
- [9] WEN J, LU Z, YANG Y, et al. Preventing stricture formation by covered esophageal stent placement after endoscopic submucosal dissection for early esophageal cancer[J]. *Dig Dis Sci*, 2014, 59(3): 658-663.
- [10] LI J J, SHAN H B, HE L J, et al. Extrasophageal saline during endoscopic submucosal dissection in a patient with early esophageal squamous cell carcinoma[J]. *Ann Thorac Surg*, 2014, 98(5): 1843-1845.
- [11] NING B, ABDELFAH M M, OTHMAN M O. Endoscopic submucosal dissection and endoscopic mucosal resection for early stage esophageal cancer[J]. *Ann Cardiothorac Surg*, 2017, 6(2): 88-98.
- [12] PROBST A, AUST D, MÄRKL B, et al. Early esophageal cancer in Europe: endoscopic treatment by endoscopic submucosal dissection[J]. *Endoscopy*, 2015, 47(2): 113-121.
- [13] ISOMOTO H, YAMAGUCHI N, MINAMI H, et al. Management of complications associated with endoscopic submucosal dissection/endoscopic mucosal resection for esophageal cancer[J]. *Dig Endosc*, 2013, 25 Suppl 1: 29-38.
- [14] 杨佳佳, 党旖旎, 彭磊, 等. 早期食管癌及高级别上皮内瘤变内镜黏膜下剥离术后非治愈性切除的危险因素分析[J]. *中华消化杂志*, 2019, 39(6): 379-383.
- [14] YANG J J, DANG Y N, PENG L, et al. Analysis of risk factors

- of non-curable resection after endoscopic submucosal dissection for early esophageal cancer and high-grade intraepithelial neoplasia[J]. Chinese Journal of Digestion, 2019, 39(6): 379-383. Chinese
- [15] 陈梦雪, 桑楠, 葛献, 等. 表浅型食管癌经内镜黏膜下剥离术导致非治愈性切除的危险因素及长期生存分析[J]. 肿瘤防治研究, 2020, 47(4): 278-282.
- [15] CHEN M X, SANG N, GE X, et al. Risk factors of non-curative resection in superficial esophageal cancer after endoscopic submucosal dissection and long-term survival analysis[J]. Cancer Research on Prevention and Treatment, 2020, 47(4): 278-282. Chinese
- [16] TOYOKAWA T, INABA T, OMOTE S, et al. Risk factors for non-curative resection of early gastric neoplasms with endoscopic submucosal dissection: analysis of 1,123 lesions[J]. Exp Ther Med, 2015, 9(4): 1209-1214.
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PAN Z G, GAO C C, XIE R. Discussion of risk factors for non-curative resection after endoscopic submucosal dissection for early esophageal cancer and high-grade intraepithelial neoplasia[J]. China Journal of Endoscopy, 2021, 27(6): 26-30. Chinese