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论著

结直肠锯齿状息肉的临床特征及中西方差异的研究

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摘要 目的:分析结直肠锯齿状息肉患者的临床特征、内镜及病理表现,并比较中西方报道的差异,旨在为结直肠锯齿状息肉诊断和治疗提供参考。方法:分析总结天津医科大学总医院消化内镜中心近年来检出的结直肠锯齿状息肉患者的内镜、病理及临床特点,并与文献报道的西方国家的数据进行比较。结果:共28981例患者进行了结肠镜检查,9191例患者至少1枚结直肠息肉。其中锯齿状息肉检出率为0.53%(153/28981),低于西方报道(1%~18%)。153例锯齿状病变中,增生性息肉(HP)、广基锯齿状腺瘤(SSA/P)、传统锯齿状腺瘤(TSA)所占比例分别为41.2%、7.2%和51.6%;而西方国家的研究显示,HP所占比例为70%~90%,SSA/P占10%~20%,TSA约占1%。锯齿状息肉在男性和年龄≥50岁的患者中检出率更高。153例锯齿状息肉中,大的锯齿状息肉(直径≥10mm)和近端锯齿状息肉所占比例分别是13.7%(21/153)和46.4%(71/153)。此外,58.2%(89/153)的锯齿状腺瘤伴有异型增生。14例锯齿状息肉伴有同时性进展性结肠肿瘤(sAN),其中大锯齿状息肉(LSPs)(OR值3.446,95%置信区间1.010-11.750, $P<0.05$)可能与伴发同时性进展性肿瘤有关。结论:结直肠锯齿状息肉检出率较低,3种亚型的比例与分布位置与西方的报道显著不同。大锯齿状息肉可能与伴发同时性进展性肿瘤的风险增加有关。

关键词 结直肠锯齿状息肉;增生性息肉;广基/传统锯齿状腺瘤;传统锯齿状腺瘤

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Clinical features of colorectal serrated polyps and the differences between China and western countries

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Abstract Objective: This study was aimed to evaluate the features of colorectal serrated polyps in a Chinese population, and analyze the differences compared with those in western countries. The purpose of this study is to provide a reference for the diagnosis and treatment of colorectal serrated polyps. **Methods:** Data from all consecutive symptomatic patients were documented from a large colonoscopy database, and were compared with those in western countries through literature review. **Results:** A total of 9191 (31.7%) patients were detected with at least one polyp. The prevalence of serrated polyps was 0.53% (153/28981), which was much lower than those in western countries (1%~18%). The proportions of hyperplastic polyp (HP), sessile serrated adenoma/polyp (SSA/P), and traditional serrated adenoma (TSA) of all serrated polyps were 41.2%, 7.2% and 51.6%, respectively, which showed a lower proportion of HP and SSA/P and a higher proportion of TSA. Western studies showed that the proportions of HP were 70%~90%, SSA/P were 10%~20%, and TSA were about 1%. Serrated polyps appeared more in males and elder patients. The proportion of large and proximal serrated polyps was 13.7% (21/153) and 46.4% (71/153), respectively. In addition, 58.2% (89/153) serrated adenomas were found with dysplasia. 14 patients with serrated polyps were found with synchronous advanced colorectal neoplasia, and large serrated polyps (LSPs) (odds ratio: 3.446, 95% confidence interval: 1.010-11.750, $P<0.05$) might have a association with synchronous advanced neoplasia (sAN). **Conclusion:** Colorectal serrated polyps have a lower detection rate in Chinese patients. The overall prevalence of colorectal serrated polyps and distribution pattern of three subtypes are significantly different in the Chinese population compared with those in western countries. LSPs might be associate with an increased risk of synchronous AN.

Key words colorectal serrated polyps; hyperplastic polyp; sessile serrated adenoma/polyp; traditional serrated adenoma

结直肠癌(colorectal cancer, CRC)是全球最常见的恶性肿瘤之一^[1]。越来越多的研究表明锯齿状息肉(serrated polyps, SPs)是CRC的癌前病变,15%~30%发生与“锯齿状通路”相关,特点是广泛的基因

失活,通过启动子区域的高甲基化(cPG岛的甲基化表型),BRAF突变和微卫星的不稳定性(MSI)导致^[2]。结直肠锯齿状息肉病理学特征为典型的锯齿状腺体,即结肠隐窝上皮的“锯齿”折叠^[1]。2010年世界卫生组织将锯齿状息肉分为3个亚型,即增生性息肉(HP)、广基锯齿状腺瘤/息肉(SSA/P)、传统锯齿状

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腺瘤(TSA),每种亚型具有不同的病理学特征和临床特征^[3]。在西方国家,锯齿状息肉同样被认为是CRC的癌前病变^[4]。尸检研究表明,25%~50%的白种人有一个或多个锯齿状病变^[5]。近期西方国家的研究结果,HP约占所有锯齿状息肉的70%~90%^[6],SSA/P占10%~20%^[7-8],TSA约占1%^[7]。随着年龄的增长,锯齿状息肉的总体检出率略有增加,这些病变在乙状结肠和直肠部位较为常见,但其分布因病理学亚型不同而不同^[9]。直径 ≤ 5 mm的HP,多分布于远端结肠和直肠^[4],与TSA的分布规律相同^[9]。SSA/P作为第二常见的锯齿状息肉,大多数位于近端结肠,包括盲肠、升结肠和横结肠^[10],并常发生在老年妇女人群中^[11]。SSA/P和HP非常难以鉴别,因其具有相似的颜色及血管分布^[12],SSA/P的诊断标准,包括平坦的表面,颜色苍白,粘液帽,隐窝底部膨大呈倒T型或者“L型”,隐窝底部的锯齿状结构,有时伴有轻度异型增生等特征^[3]。TSA是相对少见的病变,均出现异型增生^[13]。另外,大锯齿状病变,近端锯齿状息肉,与同时性进展性肿瘤相关。目前国内对结直肠锯齿状息肉临床特征的报道较少,笔者汇总了中国锯齿状息肉检出率及临床特点,并分析比较中西方差异,旨在为提高临床医师对结直肠锯齿状息肉的认识水平提供参考。

1 资料与方法

1.1 临床资料 2010年1月-2014年12月期间,因各种症状如腹痛、腹泻、排便习惯改变等,在天津医科大学总医院消化内镜中心进行结肠镜检查的患者。请经验丰富的病理医生根据WHO诊断标准将疑似结直肠锯齿状息肉的病理切片重新确认及分类^[3]。最后将所有结直肠锯齿状息肉的临床、病理数据进行收集整理,包括病人的年龄、性别、病变大小、息肉数量和发现部位等。

1.2 诊断标准 大锯齿状息肉(large serrated polyps, LSPs)被定义为直径 ≥ 10 mm的锯齿状息肉。近端息肉定位在盲肠、升结肠、肝曲、横结肠及脾曲,远端息肉定位在降结肠、乙状结肠和直肠。

1.3 排除标准 (1)年龄 < 20 岁。(2)患有各种息肉病的患者。(3)具有结直肠癌或炎症性肠病的病史。(4)具有结肠手术或息肉切除术史。(5)任何急诊结肠镜检查及内镜下治疗的患者。(6)肠道准备不充分和未到达回盲部的不完整结肠镜检查。所有的病人都签署知情同意书并接受了结肠镜检查。

1.4 器械与方法 结肠镜检查采用日本Olympus公司CF-Q260肠镜,由经验丰富的内镜医师操作。患者术前8 h口服2袋溶于2 000 mL水中的聚乙

二醇,并于2 h内喝完以行肠道准备,排泄水样便表示已做好充分肠道准备。所有收集的标本存放在10%的福尔马林液体中固定至少4 h,并用苏木精-伊红染色。根据WHO标准进行病理学分类及评价。HP的病理学特征是隐窝的上半部腔缘被覆锯齿状上皮细胞。SSA/P的典型特征是粘膜隐窝呈现锯齿状结构,隐窝基底处增宽呈倒“T”形或“L”形,锯齿状结构位于隐窝的下1/3,伴或者不伴有分支。TSA的特征是具有典型的锯齿状结构和至少一个区域可找到富含嗜酸性物质细胞质的细胞带有拉长的高柱状细胞核。具有垂直于隐窝长轴的丝状或绒毛状结构和增值出芽结构的隐窝也有助于识别TSA^[3]。

1.5 统计学分析 采用SPSS19.0软件进行统计分析。结直肠锯齿状息肉的危险因素通过检验和FISHER检验计算。均值和标准差用于计算连续变量。 $P < 0.05$ 认为差异有统计学意义。

2 结果

2.1 结直肠锯齿状息肉的检出率 从2010-2014年,共有28 981名进行过结肠镜检查患者被纳入到本研究。平均年龄为(53.2 \pm 15.0)岁,其中14 332名患者为男性,占49.5%。49.2%的患者行结肠镜检查的腹部不适,腹痛占15.9%,排便习惯改变占10.3%,腹泻占9.3%。共计有9 191人发现至少有1枚大肠息肉,149人发现至少有1枚锯齿状息肉。149例患者中共检出153枚锯齿状息肉。结直肠锯齿状息肉的检出率为0.53%(153/28 981)。其中,HP、SSA/P和TSA分别占41.2%(63/153),7.2%(11/153)和51.6%(79/153)。与西方国家相比,HP和SSA/P的比例偏低,TSA的比例偏高。

2.2 结直肠锯齿状息肉患者的临床特征分析 表1示结直肠锯齿状息肉患者的人口统计学特征。结直肠锯齿状息肉在年龄 ≥ 50 岁($\chi^2=5.593, P < 0.05$)和男性($\chi^2=4.785, P < 0.05$)患者中较多见。患者平均年龄为(57.4 \pm 13.6)岁,其中HP、SSA/P和TSA平均年龄分别为(56.2 \pm 13.0),(60.3 \pm 9.4)和(58.0 \pm 14.4)岁,但性别和年龄的亚型分布无显著性差异(表2)。图1所示,随年龄增长锯齿状腺瘤(包括SSA/P和TSA)检出率逐渐增长,而HP的检出率在60~69岁出现一个峰值。其中14例结直肠锯齿状息肉伴有同时性进展性肿瘤(sAN),其中包括大锯齿状腺瘤,合并绒毛结构腺瘤,合并重度不典型增生腺瘤和结直肠肿瘤。其中5例伴有结直肠肿瘤,1例伴有重度不典型增生,1例伴有绒毛结构,7例直径 ≥ 10 mm,表3提示大锯齿状息肉与sAN具有明显的相关性。

表 1 结直肠锯齿状息肉患者的人口统计学特征

Tab 1 Demographic characteristics of patients with colorectal serrated polyps

特点	SP	HP	SSA/P	TSA
例数	153	63	11	79
性别(男/女)	93/60	40/23	7/4	46/33
年龄(岁, $\bar{x}\pm s$)	57.4±13.6	56.2±13.0	60.3±9.4	58.0±14.4
大小/%				
≥10 mm	21(13.7)	4(6.4)	1(9.1)	16(20.3)
<10 mm	132(86.3)	59(93.6)	10(90.9)	63(79.7)
位置/%				
远端	82(53.6)	38(60.3)	5(45.5)	39(49.4)
近端	71(46.4)	25(39.7)	6(54.5)	40(50.6)
存在异型增生/%				
无	64(41.8)	59(93.7)	1(9.1)	0(0)
有	89(58.2)	4(6.3)	10(90.9)	79(100)
合并有同时性进展性结直肠肿瘤	14	4	2	8
合并≥10 mm 的腺瘤	7	1	0	6
合并有绒毛成分的腺瘤	1	1	0	0
合并有高级别上皮内瘤变的腺瘤	1	1	0	0
合并结直肠癌	5	1	2	2

表 3 结直肠锯齿状息肉伴同时性进展性肿瘤特点

Tab 3 Characteristics of colorectal serrated polyps associated with synchronous advanced neoplasia

特点	例数	SP 不伴随 sAN/例	SP 伴随 sAN/例	单变量分析		多变量分析	
				OR(95%CI)	P	OR(95%CI)	P
性别							
男	93	85	8	0.847(0.279-2.576)	0.77		
女	60	54	6				
年龄(岁, $\bar{x}\pm s$)		56.6±13.4	64.8±12.3	1.056(1.004-1.111)	0.036	1.052(0.996-1.112)	0.067
大小							
≥10 mm	21	14	7				
<10 mm	132	125	7	4.271(1.272-14.336)	0.019	3.446(1.010-11.750)	0.048
位置							
远端	82	76	6	1.608(0.530-4.880)	0.401		
近端	71	63	8				
存在异型增生							
无	64	60	4				
有	89	79	10	1.899(0.568-6.349)	0.298		
分型							
HP	63	59	4	1.251(0.690-2.266)	0.460		
SSA/P	11	9	2				
TSA	79	71	8				

2.3 SP 患者特征的中西方差异 与西方国家的结直肠锯齿状息肉以直径<5 mm 为主相似,本研究的锯齿状息肉的大小直径多小于 10 mm。LSPs 检出率 0.2%(21/9 191), 低于西方国家, 占全部锯齿状息肉 13.7%(21/153)。53.6%锯齿状息肉位于远端结肠, 60.3%HPs 位于远端结肠, 54.5% SSA/Ps 位于近端结肠, 50.6%TSAs 位于近端结肠, 在解剖位置上无明显统计学差异, 这与既往研究不同。

表 2 结直肠锯齿状息肉性别和年龄亚型分布特点

Tab 2 Gender and age subtypes of serrated colorectal polyps

项目	SP	HP/%	SSA/P/%	TSA/%	χ^2	P
性别						
男	93	40(43.0)	7(7.5)	46(49.5)	0.473	0.842
女	60	23(38.3)	4(6.7)	33(55.0)		
年龄/岁						
<50	39	18(46.2)	1(2.6)	20(51.3)	1.639	0.439
≥50	114	45(39.5)	10(8.8)	59(51.7)		
总计	153	63(41.2)	11(7.2)	79(51.6)		

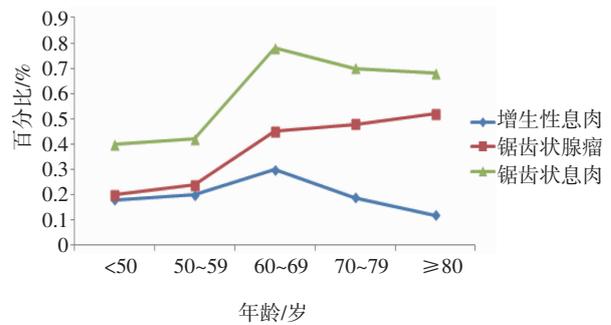


图 1 不同年龄结直肠锯齿状息肉检出率

Fig 1 Detection rates of serrated colorectal polyps at different ages

3 讨论

近年来 CRC 发病率和死亡率在全球范围内显著上升, 严重危害人类健康, 且 90% 以上的 CRC 是由癌前病变息肉恶变而来。在西方国家, 锯齿状息肉同样被认为是 CRC 的癌前病变^[4]。本研究表明, 锯齿状息肉的检出率较低, 0.53%(153/28 981), 与既往文献不同^[5,14], 其中原因可能包括锯齿状息肉的外观、发生位置不易被发现, 医生的内镜操作熟练程度

及对锯齿状息肉的认知程度不够,术前肠道准备不良等^[5]。这些也同时导致了大的锯齿状息肉(直径 ≥ 10 mm)检出率较低;但锯齿状息肉中大锯齿状息肉的比例为 13.7%与近期研究一致^[14, 16]。内镜下锯齿状息肉外观常表现为平坦的、无蒂的,常位于近端结肠^[6]。即使息肉检测率和退镜时间符合国际标准,锯齿状息肉的外观也可能导致较高的漏检率。据报道,西方国家近端结直肠锯齿状息肉的检出率在 1%和 18%之间,平均 13%^[17]。不同研究中,增生性息肉(HP)5.7%~44%^[5-6, 18-19]和广基锯齿状腺瘤/息肉(SSA/P)1%~14%^[5, 18-19]的内镜检出率也存在显著差异。中国人群的一些研究也表明广基锯齿状腺瘤/息肉(SSA/P)有很不同的检出率^[20]。多种因素包括患者群、结肠镜检查质量、病理学验证、各中心之间的差异和种族不同可能会导致这些差异^[21]。另外,病理医师与内镜医生之间的沟通不足、不明显的息肉的漏诊、缺乏对亚型分类诊断经验也导致中国患者的漏诊率。此外,饮食习惯的不同也可能导致上述差异。近期大量的研究表明,西方的饮食习惯是导致结直肠息肉高发的原因,特别是在息肉的数量和大小,以及左半结肠锯齿状腺瘤方面^[22]。但是结直肠锯齿状息肉发病率低及亚型分布不同的确切原因有待进一步研究。

与传统腺瘤的发生率随着年龄的增长而急剧增加不同,本研究分析发现锯齿状腺瘤(SSA/Ps、TSA)的发生随着年龄的增长而稳步增加,这与近期研究结果相似^[5]。其中 HPs 的检出率在 60~69 岁出现一个峰值。而另一些研究表明,年龄的增长与锯齿状息肉的检出率无显著关联^[23]。年龄是否与结直肠锯齿状息肉的检出率相关,有待进一步研究。另外本研究分析了多种因素,包括年龄、性别、息肉的大小、位置以及是否伴有不典型增生,目的是发现 sAN 的预测因子,笔者发现大锯齿状息肉与 sAN 相关。本研究也存在一些局限性:首先,当前的研究为回顾性研究。其次,目前的研究是在三级内镜中心进行的,不能忽略选择性偏差。第三,笔者的研究对象是有症状后接受结肠镜检查的患者,而西方国家数据来源可能包括平均风险报告,无症状患者年龄 ≥ 50 岁而接受肠镜筛查的数据,因此,这些不同研究之间的对比需要注意。

综上所述,本组资料结直肠锯齿状息肉检出率较低,3 种亚型的分布规律明显与西方国家研究结果不同。随着年龄增长,锯齿状腺瘤的检出率呈现稳步上升的趋势,而增生性息肉在 60~69 岁时出现一个峰值。大锯齿状息肉可能与患同时性进展性肿

瘤的风险增加有关。需要进一步的研究和评估中国人群中结直肠锯齿状息肉的检出和亚型分布情况,本文可为提高广大临床医师对结直肠锯齿状息肉的认识水平提供参考。

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