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神经内镜与显微镜下经鼻蝶入路手术切除垂体腺瘤的临床疗效比较 及术中出现脑脊液漏的危险因素分析*

陈佳 万勇 罗伟坚 陈东 赵永阳 胡继良[△]

(深圳市人民医院神经外科 广东 深圳 518000)

摘要 目的:对比垂体腺瘤患者采用显微镜或神经内镜下经鼻蝶入路手术切除后的临床疗效,分析术中出现脑脊液漏的危险因素。**方法:**回顾性分析2018年3月~2022年2月期间来我院接受手术治疗的178例垂体腺瘤患者的临床资料。根据采用手术器械的不同将178例患者分为A组(显微镜,n=91)和B组(神经内镜,n=87)。比较两组的肿瘤有效切除率、临床指标、术中脑脊液漏发生率及术后并发症发生率。根据术中是否发生脑脊液漏分为脑脊液漏组和无脑脊液漏组。经单因素和多因素Logistic回归分析患者术中发生脑脊液漏的危险因素。**结果:**B组的手术时间、住院时间短于A组,术中出血量少于A组($P<0.05$)。A组、B组的肿瘤有效切除率组间对比,无统计学差异($P>0.05$)。B组术中脑脊液漏发生率、术后并发症发生率低于A组($P<0.05$)。垂体腺瘤患者术中发生脑脊液漏与再次手术、肿瘤大小、年龄、肿瘤质地、美国麻醉医师协会(ASA)分级有关($P<0.05$)。肿瘤大小为巨大腺瘤、再次手术、肿瘤质地为韧是垂体腺瘤患者术中发生脑脊液漏的危险因素($P<0.05$)。**结论:**显微镜与神经内镜下经鼻蝶入路手术切除垂体腺瘤,治疗效果相当,但神经内镜下手术可缩短手术时间、住院时间,减少术中出血量,降低术中脑脊液漏发生率、术后并发症发生率。此外,肿瘤大小为巨大腺瘤、再次手术、肿瘤质地为韧是垂体腺瘤患者术中发生脑脊液漏的危险因素。

关键词:神经内镜;显微镜;经鼻蝶入路;垂体腺瘤;临床疗效;脑脊液漏;危险因素

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Comparison of Clinical Efficacy between Neuroendoscope and Microscope Transsphenoidal Approach Surgery for Pituitary Adenomas and Analysis of Risk Factors of Cerebrospinal Fluid Leakage during Operation*

CHEN Jia, WAN Yong, LUO Wei-jian, CHEN Dong, ZHAO Yong-yang, HU Ji-liang[△]

(Department of Neurosurgery, Shenzhen People's Hospital, Shenzhen, Guangdong, 518000, China)

ABSTRACT Objective: To compare the clinical efficacy of microscope or neuroendoscope transsphenoidal approach surgery for patients with pituitary adenomas, and to analyze the risk factors of cerebrospinal fluid leakage during operation. **Methods:** The clinical data of 178 patients with pituitary adenomas who underwent surgery in our hospital from March 2018 to February 2022 were retrospectively selected. 178 patients were divided into group A (microscope, n=91) and group B (neuroendoscope, n=87) according to different surgical instruments. The effective tumor resection rate, clinical indicators, the incidence of cerebrospinal fluid leakage during operation and the incidence of postoperative complications were compared between the two groups. According to whether cerebrospinal fluid leakage occurred during operation, it was divided into cerebrospinal fluid leakage group and no cerebrospinal fluid leakage group. The risk factors of cerebrospinal fluid leakage during operation were analyzed by univariate and multivariate Logistic regression. **Results:** The operation time and hospital stay of the group B were shorter than those of the group A, and the amount of intraoperative bleeding was less than that of the group A ($P<0.05$). There was no significant difference in the effective tumor resection rate between group A and group B ($P>0.05$). The incidence of cerebrospinal fluid leakage during operation and postoperative complications of the group B were lower than those of the group A ($P<0.05$). Cerebrospinal fluid leakage during operation in patients with pituitary adenoma was related to reoperation, tumor size, age, tumor texture, American Association of anesthesiologists (ASA) grade ($P<0.05$). The tumor size was huge adenoma, reoperation, and the tumor texture was tough were the risk factors for cerebrospinal fluid leakage during operation in patients with pituitary adenoma ($P<0.05$). **Conclusion:** Microscope and neuroendoscope transsphenoidal surgery for pituitary adenomas has the same therapeutic effect, but neuroendoscope surgery can shorten the operation time, hospital stay, reduce the amount of intraoperative bleeding, reduce the incidence of cerebrospinal fluid leakage during operation and postoperative complications. In addition, the tumor size is huge adenoma, reoperation, and the tumor texture is tough are the risk factors of cerebrospinal fluid leakage during operation in patients with pituitary adenoma.

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作者简介:陈佳(1984-),男,硕士,主治医师,研究方向:颅底肿瘤、颅内血管病、垂体瘤, E-mail: Lc-jervis@163.com

[△] 通讯作者:胡继良(1975-),男,博士,主任医师,研究方向:神经内镜、显微镜颅脑肿瘤手术治疗, E-mail: hujlsz@126.com

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Key words: Neuroendoscope; Microscope; Transsphenoidal approach; Pituitary adenoma; Clinical efficacy; Cerebrospinal fluid leakage; Risk factors

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前言

垂体腺瘤是属于内分泌系统的一种肿瘤,居颅内肿瘤的第二位^[1]。现临床针对垂体腺瘤患者的治疗均首选手术切除,主要为经鼻蝶入路手术切除肿瘤^[2]。显微镜是以往经鼻蝶入路手术切除肿瘤常用的器械之一,近年来随着新手术器械的研发应用,内镜神经外科技术的进步,内镜手术应用范围不断扩大,神经内镜下经鼻蝶入路手术切除垂体腺瘤的手术也日益增多,但有关两种器械下进行手术切除孰优孰劣尚无定论^[3]。脑脊液漏是垂体腺瘤患者术中常见的并发症,患者术中出现脑脊液漏可能会带来颅内感染、气颅等一系列不良后果,不利于患者术后恢复^[4,5]。基于此,本研究通过对比两种器械下经鼻蝶入路手术切除垂体腺瘤的治疗效果,并分析术中出现脑脊液漏的危险因素,旨在为临床垂体腺瘤预后改善提供数据支持。

1 资料与方法

1.1 基线资料

回顾性分析 2018 年 3 月~2022 年 2 月期间来我院接受手术治疗的 178 例垂体腺瘤患者的临床资料。纳入标准:(1)诊断符合《中国垂体腺瘤外科治疗专家共识》^[6],表现为视野缺损、库欣综合征、头痛、肢端肥大症、垂体坏死、女性异常闭经、溢乳、视力下降、出血及脑膜刺激症状,后经蝶鞍项检查、内分泌学检查、CT 检查等确诊;(2)均符合手术指征,手术操作由同一组医师完成。排除标准:(1)孕妇或妊娠期妇女;(2)合并精神疾病,无法配合者;(3)近期曾接受过药物内分泌治疗者;(4)合并心、肝、肾等严重原发性疾病者。根据采用手术器械的不同将 178 例患者分为 A 组(显微镜,n=91)和 B 组(神经内镜,n=87)。A 组:男 52 例,女 39 例,病理类型:巨大腺瘤(肿瘤直径>3 cm)22 例,大腺瘤(1 cm≤肿瘤直径≤3 cm)36 例,微腺瘤(肿瘤直径<1 cm)33 例;年龄 18~69 岁,平均年龄(39.72±5.18)岁。B 组:男 44 例,女 43 例,病理类型:巨大腺瘤 24 例,大腺瘤 32

例,微腺瘤 31 例;年龄 20~71 岁,平均年龄(40.06±4.93)岁。两组一般资料比较,无差异($P>0.05$),具有可比性。

1.2 方法

两组均进行经鼻蝶入路手术切除,A 组在显微镜下进行手术操作。具体方案如下:取仰卧位,全麻,分离鼻中隔黏膜,开放鞍底骨质及蝶窦,若肿瘤为微腺瘤,可沿着瘤壁将肿瘤分离。若肿瘤为巨大腺瘤、大腺瘤,先吸刮局部肿瘤,再由下往上逐层切除肿瘤组织。B 组在神经内镜下进行手术。具体方案如下:取仰卧位,全麻,头部后仰约 20°,借助吸引器、取瘤钳及刮匙将鞍内肿瘤切除。

1.3 观察指标

(1)记录两组术中出血量、手术时间及住院时间。(2)记录两组肿瘤有效切除率及术后并发症(包括颅内感染、电解质紊乱、脑脊液漏)发生率,有效切除标准参照《中国垂体腺瘤外科治疗专家共识》^[6]。(3)记录两组术中脑脊液漏发生率,根据术中是否发生脑脊液漏分脑脊液漏组和无脑脊液漏组。(4)根据病历资料获取再次手术、年龄、分泌类型(泌乳素(PRL)、生长激素(GH)、促肾上腺皮质激素(ACTH)、促甲状腺素(TSH)、无功能)、体质量指数(BMI)、合并疾病(高血压、糖尿病、冠心病、慢性呼吸系统疾病)、性别、美国麻醉医师协会(ASA)分级、肿瘤质地、肿瘤大小等资料。

1.4 统计学方法

本研究的统计学分析采用 SPSS21.0 统计软件,计量资料以($\bar{x}\pm s$)表示,采用 t 检验。计数资料采用率表示,行 χ^2 检验。患者术中发生脑脊液漏的危险因素经多因素 Logistic 回归分析,检验标准 $\alpha=0.05$ 。

2 结果

2.1 两组临床指标对比

与 A 组相比,B 组的住院时间、手术时间缩短,手术出血量减少($P<0.05$),见表 1。

表 1 两组临床指标对比($\bar{x}\pm s$)

Table 1 Comparison of clinical indicators between the two groups($\bar{x}\pm s$)

Groups	Operation time(min)	Amount of intraoperative bleeding(mL)	Hospital stay(d)
Group A(n=91)	109.24±14.68	68.79±6.57	8.77±0.61
Group B(n=87)	87.16±13.39	53.06±5.88	6.91±0.53
t	10.470	16.805	21.675
P	0.000	0.000	0.000

2.2 两组肿瘤有效切除率、术中脑脊液漏发生率及术后并发症发生率对比

两组肿瘤有效切除率组间对比未见差异($P>0.05$)。B 组术中脑脊液漏发生率、术后并发症发生率低于 A 组($P<0.05$),见表 2。

2.3 单因素分析

根据术中是否发生脑脊液漏分组:脑脊液漏组(n=29)和无脑脊液漏组(n=149)。单因素分析结果显示:垂体腺瘤患者术中发生脑脊液漏与 ASA 分级、年龄、肿瘤大小、肿瘤质地、再次手术有关($P<0.05$),而与 BMI、合并高血压、性别、合并糖尿病、分泌类型、合并冠心病、合并慢性呼吸系统疾病无关($P>0.05$),见表 3。

表 2 两组肿瘤有效切除率、术中脑脊液漏发生率及术后并发症发生率对比(n,%)

Table 2 Comparison of effective tumor resection rate, intraoperative cerebrospinal fluid leakage rate and postoperative complication rate between the two groups [n(%)]

Groups	Effective tumor resection rate	Incidence of cerebrospinal fluid leakage during operation	Incidence of postoperative complications			Total incidence rate
			Intracranial infection	Electrolyte disorder	Cerebrospinal fluid leakage	
Group A(n=91)	87(95.60)	20(21.98)	2(2.20)	5(5.49)	5(5.49)	12(13.19)
Group B(n=87)	84(96.55)	9(10.34)	1(1.15)	2(2.30)	1(1.15)	4(4.60)
χ^2	0.106	4.414				4.011
<i>P</i>	0.745	0.036				0.045

表 3 单因素分析

Table 3 Univariate analysis(n, %)

Factors		Cerebrospinal fluid leakage group(n=29)	No cerebrospinal fluid leakage group(n=149)	χ^2	<i>P</i>
Age(years)	<60	20(68.97)	59(39.60)	8.482	0.004
	≥60	9(31.03)	90(60.40)		
Gender	Male	16(55.17)	80(53.69)	0.021	0.884
	Female	13(44.83)	69(46.31)		
Tumor size	Microadenoma	6(20.69)	58(38.92)	9.458	0.009
	Macroadenoma	9(31.03)	59(39.60)		
	Huge adenoma	14(48.28)	32(21.48)		
Reoperation	Yes	21(72.41)	51(34.23)	14.695	0.000
	No	8(27.59)	98(65.77)		
Secretory type	PRL	6(20.69)	25(16.78)	1.672	0.797
	GH	7(24.14)	28(18.79)		
	ACTH	6(20.69)	26(17.45)		
	TSH	0(0.00)	1(0.67)		
	No function	10(34.48)	69(46.31)		
BMI(kg/m ²)	≤24	7(24.14)	61(40.94)	4.194	0.123
	24~28	9(31.03)	47(31.54)		
	≥28	13(44.83)	41(27.52)		
Complicated with hypertension		7(24.14)	19(12.75)	2.523	0.112
Complicated with diabetes		5(17.24)	11(7.38)	2.884	0.089
Complicated with coronary heart disease		4(13.79)	9(6.04)	2.155	0.142
Complicated with chronic respiratory diseases		6(20.69)	13(8.72)	3.645	0.056
ASA grade	I grade	7(24.13)	69(46.31)	9.706	0.007
	II grade	8(27.59)	48(32.21)		
	III grade	14(48.28)	32(21.48)		
Tumor texture	Tough	23(79.31)	47(31.54)	23.123	0.000
	Soft	6(20.69)	102(68.46)		

2.4 多因素分析

以垂体腺瘤患者术中是否发生脑脊液漏作为因变量(未发生=0,发生=1),以肿瘤大小、年龄、再次手术、ASA 分级、肿瘤质地作为自变量,赋值情况见表 4。结果显示:肿瘤大小为巨大

腺瘤、再次手术、肿瘤质地为韧是垂体腺瘤患者术中发生脑脊液漏的危险因素($P<0.05$)。见表 5。

3 讨论

表 4 赋值情况
Table 4 Assignment situation

Factors	Assignment
Age	< 60 years=0, ≥ 60 years=1
Tumor size	Microadenoma=0, macroadenoma=1, huge adenoma=2
Reoperation	No=0, yes=1
ASA grade	I grade=0, II grade=1, III grade=2
Tumor texture	Soft=0, tough=1

表 5 垂体腺瘤患者术中发生脑脊液漏的多因素分析
Table 5 Multifactor analysis of cerebrospinal fluid leakage in patients with pituitary adenoma during operation

Indicators	β	SE	Wald χ^2	P	OR	95%CI
Tumor size was huge adenoma	0.336	0.294	8.639	0.000	1.562	1.318~1.827
Reoperation	0.298	0.237	7.268	0.001	1.381	1.143~1.581
Tumor texture was tough	0.324	0.251	8.163	0.000	1.446	1.289~1.607

垂体腺瘤的治疗方案包括放疗、药物治疗和手术治疗等,其中放疗因并发症较多受到临床广泛使用限制,而药物治疗仅为手术和放疗的辅助手段,因此,手术已成为垂体腺瘤患者的首选方案,主要采用经鼻蝶入路^[7-9]。神经内镜与显微镜下完成手术操作均是现今常用的手术方式,两种手术各有利弊。显微镜下经鼻蝶入路手术方式的优点在于:手术可双手操作,止血简单、方便;显微镜提供的是三维视野,双眼直视下空间立体感较强,具有清晰的术野信息^[10];显微镜手术开展较早,具有丰富的临床应用经验,学习曲线短。而其缺点则主要是显微镜术野信息固定,在进行鞍上及后外侧的手术操作时,无法较好地暴露蝶鞍区的解剖情况^[11]。同时,显微镜下进行手术操作时需将鼻中隔推向对侧,操作不当易导致人工骨折,增加术中出血量,提高并发症发生风险^[12]。神经内镜下完成手术操作的优势在于:内镜下具有广角照明和全景视野,能够更为清晰直观的纵观手术视野;同时神经内镜体积小,对人体的损伤也相对更轻^[13-15],因此本文通过对比两种器械经鼻蝶入路手术切除垂体腺瘤的临床疗效,以期临床手术入路的选择提供参考。

从本研究的结果来看,两种器械下经鼻蝶入路手术切除垂体腺瘤,肿瘤有效切除率相当,但神经内镜下手术的患者其手术时间、住院时间明显短于显微镜下手术患者,术中出血量也相对更少,其原因可能是医师在掌握神经内镜的操作后,手术操作变得更为简单、方便,术中无需将鼻中隔隔断、黏膜等进行分离,明显减少手术用时,减少术中损伤,有利于患者术后恢复,缩短住院时间^[16,17]。研究结果还显示,神经内镜下手术术中脑脊液漏发生率、术后并发症发生率较低。可能是神经内镜可全方位观察蝶窦内的情况,有助于减少患者术后出现并发症的风险有关^[18,19]。垂体腺瘤起源于蛛网膜外的垂体组织内^[20],理论上在整个手术操作过程中,可以完全在蛛网膜外将垂体瘤切除而不需进入蛛网膜下腔,但有临床报道显示^[21-23],手术过程中可发生不同程度的脑脊液漏。本次研究显示,178 例接受手术的患者中,约有 29 例术中发生脑脊液漏,发生率为 16.29%。故本次研究针对患者发生脑脊液漏的相关因素进行分析,结果显

示:肿瘤大小为巨大腺瘤、再次手术、肿瘤质地为韧是垂体腺瘤患者术中发生脑脊液漏的危险因素,依次分析原因,巨大腺瘤通常会使鞍鞍扩大,并压迫侵袭鞍隔,故而在手术期间,更易造成鞍隔损伤^[24];待大部分肿瘤切除后,蛛网膜更易被损伤,提高了术中脑脊液漏发生风险^[25]。而再次手术时肿瘤组织与正常垂体间边界模糊,与鞍隔黏连,切除肿瘤过程中导致鞍隔破损,增加了术中脑脊液漏发生风险^[4,26]。肿瘤质地为韧提示肿瘤恶性程度高,切除难度大,更易增加并发症发生风险^[27]。

综上所述,显微镜与神经内镜下经鼻蝶入路手术切除垂体腺瘤,治疗效果相当,但神经内镜下手术在缩短手术时间、住院时间,减少术中出血量,降低术中脑脊液漏发生率、术后并发症发生率方面的作用更为突出。此外,肿瘤大小为巨大腺瘤、再次手术、肿瘤质地为韧是垂体腺瘤患者术中发生脑脊液漏的危险因素,应重视此类患者的围术期处理,以减少术中脑脊液漏的发生率。

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