

· 听神经瘤 ·

听神经瘤乙状窦后入路手术后迟发性面瘫影响因素分析

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【摘要】目的 总结听神经瘤手术后迟发性面瘫发生特点并筛查相关影响因素。**方法** 纳入2019年1月至2021年5月郑州大学第一附属医院诊断与治疗的171例听神经瘤患者,均于神经电生理监测下行乙状窦后入路手术,手术前后采用面神经功能House-Brackmann(H-B)分级进行面瘫分级,单因素和多因素前进法Logistic回归分析筛查听神经瘤手术后迟发性面瘫相关危险因素。**结果** 根据术后是否发生迟发性面瘫分为迟发性面瘫组(DFP组,19例)和非迟发性面瘫组(NDFP组,152例),DFP组肿瘤直径小于NDFP组($t = 6.623, P = 0.001$)、小瘤体比例($\chi^2 = 18.585, P = 0.000$)及肿瘤与面神经轻度粘连比例($\chi^2 = 21.442, P = 0.000$)均高于NDFP组。Logistic回归分析显示,小瘤体($OR = 15.797, 95\%CI: 3.324 \sim 75.081; P = 0.001$)及肿瘤与面神经轻度粘连($OR = 11.690, 95\%CI: 3.413 \sim 40.042; P = 0.000$)是听神经瘤手术后迟发性面瘫的危险因素。随访至术后1年,19例迟发性面瘫患者中17例面神经功能正常或接近正常(H-B分级I~II级)。**结论** 肿瘤体积较小以及肿瘤与面神经轻度粘连的患者术后易发生迟发性面瘫,此类患者面神经功能预后良好。

【关键词】 神经瘤, 听; 显微外科手术; 面神经麻痹; 手术后并发症; 危险因素; Logistic模型

Analysis of influencing factors of delayed facial paralysis after retrosigmoid approach surgery for vestibular schwannoma

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【Abstract】 **Objective** To summarize the characteristics of delayed facial paralysis (DFP) after retrosigmoid approach surgery for vestibular schwannoma and screen its related influencing factors. **Methods** A total of 171 patients with vestibular schwannoma treated in The First Affiliated Hospital of Zhengzhou University from January 2019 to May 2021 were included in the study. All patients underwent retrosigmoid approach surgery under neuroelectrophysiological monitoring. Before and after the surgery, facial paralysis was classified according to House - Brackmann (H - B) grade of facial nerve function. Univariate and multivariate forward Logistic regression analysis was used to screen related risk factors of DFP after vestibular schwannoma surgery. **Results** Patients were divided into DFP group ($n = 19$) and non-DFP (NDFP) group ($n = 152$) according to whether there was DFP after surgery. The tumor diameter in DFP group was smaller than that in NDFP group ($t = 6.623, P = 0.001$), the proportion of small tumors ($\chi^2 = 18.585, P = 0.000$) and the proportion of slight adhesion between tumor and facial nerve ($\chi^2 = 21.442, P = 0.000$) were higher than those in NDFP group. Logistic regression analysis showed small tumor ($OR = 15.797, 95\%CI: 3.324 \sim 75.081; P = 0.001$) and slight adhesion between tumor and facial nerve ($OR = 11.690, 95\%CI: 3.413 \sim 40.042; P = 0.000$) were risk factors for DFP after vestibular schwannoma surgery. Following up to one year after surgery, the recovery rate of facial nerve function (H-B grade I - II) in DFP group was 17/19. **Conclusions** The patients with small tumor volume and slight adhesion between tumor and facial nerve are prone to DFP, and the prognosis of facial nerve function in such patients is good.

【Key words】 Neuroma, acoustic; Microsurgery; Facial paralysis; Postoperative complications; Risk factors; Logistic models

Conflicts of interest: none declared

听神经瘤是起源于前庭蜗神经施万细胞、生长缓慢的良性肿瘤,其直径每年仅增长1 mm^[1-2],约占全部颅内肿瘤的5%,发病率为1/10万^[3],确诊年龄通常为50~60岁^[4-7]。临床主要表现为单侧听力下降、耳鸣、眩晕、面肌无力麻木、脑脊液漏、脑膜炎、缺血性卒中等^[8];肿瘤进展还可导致构音障碍、吞咽困难和脑积水等症状或体征^[9-10]。手术切除为主要治疗方法,尽管已在面神经解剖保留方面取得实质性进展,但术后出现的不同程度面神经麻痹始终困扰术者和患者^[11-12]。严重的面神经麻痹可以导致面瘫、眼部疾病和生活质量下降^[13],既往研究侧重于术后即时和长期面瘫,较少关注迟发性面瘫(DFP)。本研究拟对郑州大学第一附属医院神经外科近3年诊断与治疗的171例听神经瘤患者术后迟发性面瘫的发生特点进行回顾分析,并筛查相关影响因素,以为临床预防迟发性面瘫提供依据。

对象与方法

一、研究对象

1. 纳入与排除标准 (1)单侧脑桥小脑角(CPA)区占位性病变。(2)采取乙状窦后入路手术,并经术后病理证实为神经鞘瘤。(3)术前面神经功能正常[House-Brackmann(H-B)分级<Ⅱ级]。(4)排除伴发以下情况的病例:Ⅱ型神经纤维瘤病(NF2)、既往曾行放射治疗或后颅窝手术、术前即存在面神经功能障碍(H-B分级≥Ⅱ级)。(5)所有患者及其家属均对手术方案和风险知情并签署知情同意书。

2. 一般资料 选择2019年1月至2021年5月在我院神经外科住院治疗的听神经瘤患者共171例,男性82例,女性89例;年龄31~63岁,平均(46.26±9.27)岁。临床主要表现为听力下降或耳鸣(158例占92.40%)、头晕(12例占7.02%)、三叉神经功能障碍(2例占1.17%)。

二、研究方法

1. 乙状窦后入路手术 患者侧卧位,气管插管全身麻醉,DORO头架(德国PMI公司)固定头部,连接面神经电生理监测仪。采取乙状窦后入路,耳后发际内直切口,长度约10 cm,剪开硬脑膜,开放枕

大池并缓慢释放脑脊液,降低颅内压以获得手术操作空间,以0.10 mA刺激副神经,若斜方肌呈现动作电位,证明参数设置正确、探头无故障以及无肌松药的影响,再以1 mA刺激肿瘤周围,若无面神经支配肌肉动作电位,证明刺激点距离面神经较远。先行瘤内减压,再沿肿瘤包膜锐性游离并切除肿瘤,尽量避免损伤周围血管、神经,继续磨除内听道后壁骨质,切除内听道内肿瘤。根据术中电生理监测反应幅度决定手术切除程度,分离过程中间断予以0.20 mA重复刺激,若出现肌电振幅显著下降则停止分离切除,同时评估肿瘤与面神经粘连程度,轻度粘连定义为肿瘤与面神经较易分离,面神经无压迫或受压变扁平,二者之间有明显分离界面;重度粘连定义为肿瘤与面神经不易分离,面神经受压膜化,或二者之间无分离界面^[14]。

2. 围手术期MRI检查 采用德国Siemens公司生产的Prisma 3.0T MRI扫描仪,标准20通道头部线圈。术前MRI平扫和动态增强扫描观察肿瘤侧别、直径和性质,肿瘤直径为横断面增强T₁WI图像上测量的肿瘤最大径(包括内听道内肿瘤),直径≥30 mm定义为大瘤体、<30 mm为小瘤体;肿瘤性质分为实性和囊实性,横断面增强T₁WI显示囊性成分体积≥肿瘤体积的1/3为囊实性、<肿瘤体积的1/3为实性。术后7 d内行MRI增强扫描,观察肿瘤切除程度即肿瘤全切除或未全切除,后者包括近全切除(肿瘤残留<5%)、次全切除(肿瘤残留5%~10%)和部分切除(肿瘤残留>10%)。

3. 面神经功能评价 手术前后采用面神经功能H-B分级^[15]进行面瘫分级:I级,各区域面肌运动正常;Ⅱ级,仔细观察有轻度面肌无力和非常轻微的联带运动,静止状态面部对称,肌张力正常,运动状态额部正常,稍用力闭眼完全,口角轻度不对称;Ⅲ级,有明显的面肌无力症状但无面部变形,有明显的联带运动或面肌痉挛,静止状态面部对称,肌张力正常,运动状态额部运动减弱,用力闭眼完全,最大用力时可见口角轻度不对称;Ⅳ级,有明显的面肌无力或面部变形,静止状态面部对称,肌张力正常,运动状态无额部运动,闭眼不完全,最大用力



图1 女性患者,39岁。临床诊断为听神经瘤,采取乙状窦后入路手术,术后次日发生迟发性面瘫 1a 术前横断面抑脂增强T₁WI显示,右侧脑桥小脑角区占位性病变呈不均匀强化(箭头所示) 1b 术中可见肿瘤组织与面神经轻度粘连,面神经受压稍变扁平 1c 术后7d横断面抑脂增强T₁WI显示无肿瘤残留

Figure 1 A 39-year-old female patient diagnosed as vestibular schwannoma, underwent vestibular schwannoma resection via retrosigmoid approach, and DFP occurred on the second day after surgery. Preoperative axial fat suppression enhanced T₁WI showed occupied lesions in the right CPA with uneven enhancement (arrow indicates, Panel 1a). Slight adhesion between the tumor tissue and the facial nerve was seen during surgery, the facial nerve was compressed and slightly flattened (Panel 1b). Seven days after surgery, axial fat suppression enhanced T₁WI showed no residual tumor (Panel 1c).

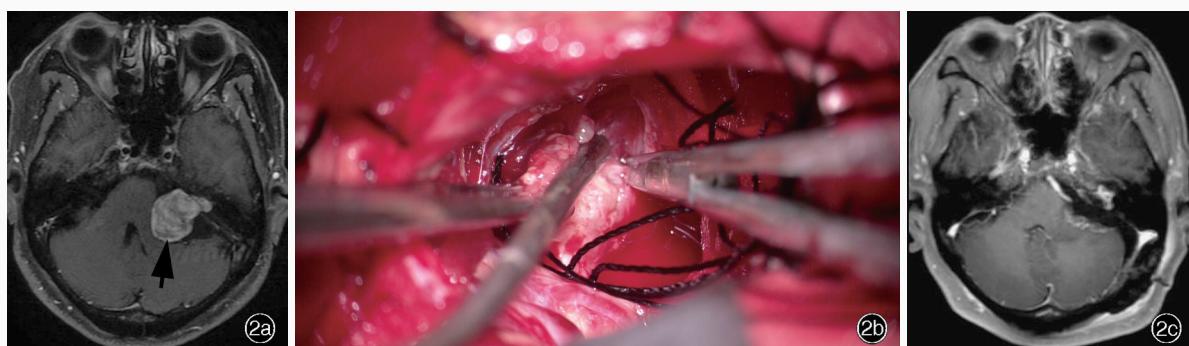


图2 女性患者,65岁。临床诊断为听神经瘤,采取乙状窦后入路手术,术后即刻发生面瘫 2a 术前横断面抑脂增强T₁WI显示,右侧脑桥小脑角区占位性病变呈不均匀强化(箭头所示) 2b 术中可见肿瘤组织与面神经重度粘连,二者之间无明显分离界面 2c 术后7d横断面增强T₁WI显示无肿瘤残留

Figure 2 A 65-year-old female patient diagnosed as vestibular schwannoma, underwent vestibular schwannoma resection via retrosigmoid approach, and DFP occurred immediately after the surgery. Preoperative axial fat suppression enhanced T₁WI showed occupied lesions in the right CPA with uneven enhancement (arrow indicates, Panel 2a). Severe adhesion between the tumor tissue and the facial nerve was seen during the surgery, without obvious separation interface (Panel 2b). Seven days after surgery, axial enhanced T₁WI showed no residual tumor (Panel 2c).

时可见口角不对称;V级,仅存在几乎无法察觉的面部运动,静止状态面部不对称,运动状态无额部运动,闭眼不完全,口角轻微运动;VI级,完全性面肌麻痹,无面部运动。与术后即刻相比,术后1个月内面瘫分级恶化≥1级,定义为迟发性面瘫。随访至术后1年,记录面神经功能恢复率(H-B分级I~II级)。

4. 统计分析方法 采用SPSS 26.0统计软件进行数据处理与分析。计数资料以相对数构成比(%)或率(%)表示,采用χ²检验。呈正态分布的计量资料以均数±标准差($\bar{x} \pm s$)表示,行两独立样本的t检验;呈非正态分布的计量资料以中位数和四分位数间距 [$M(P_{25}, P_{75})$] 表示,采用Mann-Whitney U检验。听神经瘤乙状窦后入路手术后迟发性面瘫相关危

险因素的筛查采用单因素和多因素前进法Logistic回归分析($\alpha_{入}=0.05, \alpha_{出}=0.10$)。以 $P \leq 0.05$ 为差异具有统计学意义。

结 果

本组患者肿瘤位于左侧85例(49.71%)、右侧86例(50.29%);肿瘤直径16~49 mm,平均(33.02±8.45) mm;呈大瘤体97例(56.73%),小瘤体74例(43.27%);肿瘤呈囊实性86例(50.29%),实性85例(49.71%)。术中可见肿瘤与面神经轻度粘连55例(32.16%,图1)、重度粘连116例(67.84%,图2);肿瘤全切除131例(76.61%)、未全切除40例(23.39%)。术后即刻H-B分级I级41例(23.98%)、II级57例(33.33%)、III级52例(30.41%)、IV级18例

表1 DFP组与NDFP组患者临床资料的比较**Table 1.** Comparison of clinical data between DFP group and NDFP group

观察指标	DFP组 (n=19)	NDFP组 (n=152)	χ^2 或t值	P值	观察指标	DFP组 (n=19)	NDFP组 (n=152)	χ^2 或t值	P值
性别[例(%)]			0.187	0.665	肿瘤与面神经粘连程度[例(%)]			21.442	0.000
男性	10(10/19)	72(47.37)			轻度粘连	15(15/19)	40(26.32)		
女性	9(9/19)	80(52.63)			重度粘连	4(4/19)	112(73.68)		
年龄($\bar{x} \pm s$,岁)	41.73 ± 9.50	46.26 ± 9.28	10.254	0.988	肿瘤切除程度[例(%)]			0.295	0.587
肿瘤侧别[例(%)]			2.810	0.094	全切除	16(16/19)	115(75.66)		
左侧	6(6/19)	79(51.97)			未全切除	3(3/19)	37(24.34)		
右侧	13(13/19)	73(48.03)			术后即刻H-B分级[例(%)]			-0.779	0.436
肿瘤直径($\bar{x} \pm s$,mm)	20.74 ± 2.68	34.55 ± 7.62	6.623	0.001	I级	5(5/19)	36(23.68)		
肿瘤大小[例(%)]			18.585	0.000	II级	8(8/19)	49(32.24)		
大瘤体	2(2/19)	95(62.50)			III级	4(4/19)	48(31.58)		
小瘤体	17(17/19)	57(37.50)			IV级	2(2/19)	16(10.53)		
肿瘤性质[例(%)]			0.494	0.482	V级	0(0/19)	2(1.32)		
囊实性	11(11/19)	75(49.34)			VI级	0(0/19)	1(0.66)		
实性	8(8/19)	77(50.66)							

Two-independent-sample t test for comparison of age and tumor diameter, and χ^2 test for comparison of others, 年龄和肿瘤直径的比较行两独立样本的t检验,其余指标的比较行 χ^2 检验。DFP, delayed facial paralysis, 迟发性面瘫; NDFP, non delayed facial paralysis, 非迟发性面瘫; H-B, House-Brackmann 分级

(10.53%)、V级2例(1.17%)、VI级1例(0.58%)。术后1个月内19例(11.11%)患者发生迟发性面瘫(DFP组),152例(88.89%)未发生迟发性面瘫(NDFP组),DFP组肿瘤直径小于NDFP组($P = 0.001$)、小瘤体比例($P = 0.000$)及肿瘤与面神经轻度粘连比例($P = 0.000$)高于NDFP组,其他指标组间差异无统计学意义(均 $P > 0.05$,表1)。随访至术后1年,126例(73.68%)面神经功能恢复(H-B分级为I~II级),DFP组17例(17/19)、NDFP组109例(71.71%),组间差异未达到统计学意义($\chi^2 = 2.748$, $P = 0.097$)。

单因素Logistic回归分析显示,小瘤体($P = 0.023$)及肿瘤与面神经轻度粘连($P = 0.000$)是听神经瘤手术后出现迟发性面瘫的相关影响因素(表2,3)。根据纳入与剔除标准,将上述因素代入多因素Logistic回归方程,结果显示,小瘤体($OR = 15.797$,95%CI:3.324~75.081; $P = 0.001$)及肿瘤与面神经轻度粘连($OR = 11.690$,95%CI:3.413~40.042; $P = 0.000$)是听神经瘤手术后出现迟发性面瘫的危险因素(表4)。

讨 论

听神经瘤手术后迟发性面瘫的定义尚未达成

共识,从而使得各文献报道的发病率不尽一致,Tawfik等^[16]认为听神经瘤术后迟发性面瘫的总体发病率约4.8%;Lalwani等^[17]报告为41%;与术后即刻面瘫相对而言,本研究将术后1个月内面神经功能H-B分级恶化≥1级定义为迟发性面瘫,发病率约11.11%(19/171),与Carlstrom等^[18]报告的5%~30%相符。迟发性面瘫的发病机制尚不明确,有学者认为,水痘-带状疱疹病毒(VZV)或单纯疱疹病毒(HSV)IgM滴度升高与之相关,提示病毒再激活在其发病机制中发挥重要作用^[19]。单纯疱疹病毒再激活、血管痉挛致相关神经缺血、手术创伤致面神经细胞凋亡或热损伤、无菌性蛛网膜炎均可能是迟发性面瘫的诱发因素,但目前均无足够证据^[20]。肿瘤大小与术后迟发性面瘫的相关研究较少,Carlstrom等^[18]的队列研究共纳入368例听神经瘤患者,其中60例(16.30%)于术后5~30天H-B分级恶化≥2级,但是并未发现肿瘤大小是影响术后迟发性面瘫的危险因素。Morton等^[21]手术切除104例听神经瘤,对术后即刻出现面神经麻痹定义为即刻性面瘫(IFP);术前和术后即刻面神经功能正常而术后1~30天出现面神经麻痹定义为迟发性面瘫,结果显示,9例(8.65%)术后发生即刻性面瘫、26例(25%)发生迟发性面瘫、余69例(66.35%)未发生面

表2 听神经瘤手术后迟发性面瘫相关影响因素的变量赋值表**Table 2.** Variable assignment of related influencing factors of DFP after vestibular schwannoma surgery

变量	赋值	
	0	1
术后迟发性面瘫	否	是
性别	女性	男性
肿瘤侧别	左侧	右侧
瘤体大小	大瘤体	小瘤体
肿瘤性质	囊实性	实性
肿瘤与面神经粘连程度	重度粘连	轻度粘连
肿瘤切除程度	未全切除	全切除

表3 听神经瘤手术后迟发性面瘫相关影响因素的单因素Logistic回归分析**Table 3.** Univariate Logistic regression analysis of related influencing factors of DFP after vestibular schwannoma surgery

变量	b	SE	Wald χ^2	P值	OR值	OR 95%CI
男性	0.971	1.166	0.693	0.405	2.639	0.269~25.918
年龄	0.019	0.039	0.241	0.623	1.019	0.944~1.101
肿瘤位于右侧	2.776	1.183	5.510	0.099	16.060	1.581~13.128
小瘤体	1.809	0.793	5.196	0.023	6.101	1.288~28.893
肿瘤呈实性	-2.309	1.027	5.052	0.065	0.099	0.013~0.744
肿瘤与面神经 轻度粘连	-2.450	0.605	16.422	0.000	0.086	0.026~0.282
肿瘤全切除	2.574	1.369	3.535	0.060	13.115	0.896~11.856

表4 听神经瘤手术后迟发性面瘫相关影响因素的多因素前进法Logistic回归分析**Table 4.** Multivariate forward Logistic regression analysis of related influencing factors of DFP after vestibular schwannoma surgery

变量	b	SE	Wald χ^2	P值	OR值	OR 95%CI
小瘤体	2.760	0.795	12.042	0.001	15.797	3.324~75.081
肿瘤与面神经 轻度粘连	2.459	0.628	15.320	0.000	11.690	3.413~40.042
常数项	0.020	0.377	0.003	0.958		

瘫,即刻性面瘫患者肿瘤直径大于迟发性面瘫和无面瘫患者,术中面神经反应小于无面瘫患者。本研究迟发性面瘫患者肿瘤直径小于、小瘤体比例高于非迟发性面瘫患者;进一步行 Logistic 回归分析,小瘤体是术后出现迟发性面瘫的危险因素。目前尚无肿瘤与面神经粘连程度是术后迟发性面瘫危险因素的报道,本研究首次对二者关系进行分析,结果显示,迟发性面瘫患者肿瘤与面神经轻度粘连比例高于非迟发性面瘫患者,Logistic 回归分析显示,肿瘤与面神经轻度粘连是术后发生迟发性面瘫的

危险因素。

本研究还发现,随访至术后1年,19例迟发性面瘫患者中有17例面神经功能恢复正常或接近正常(H-B分级I~II级),面神经功能恢复率高于非迟发性面瘫患者,但差异并未达到统计学意义[17/19对71.71%(109/152); $\chi^2=2.748, P=0.097$]。既往文献报道,迟发性面瘫预后较好,81%~100%患者面神经功能可恢复正常或接近正常^[18,21],与本研究结果相近,虽然大多数患者远期预后较好,但仍是听神经瘤手术后引起患者生活质量下降的重要因素。

综上所述,肿瘤体积较小、肿瘤与面神经轻度粘连的听神经瘤患者术后易发生迟发性面瘫。然而,本研究为单中心回顾性研究,且由于2019年以前并未关注听神经瘤手术后迟发性面瘫,因此所纳入患者均为2019年以后病例,样本量较小,使统计分析易受抽样误差的影响,今后尚待扩大样本量、持续随访,进一步开展多中心临床研究加以验证。

利益冲突 无

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· 小词典 ·

中英文对照名词词汇(二)

慢性进行性眼外肌麻痹	chronic progressive external ophthalmoplegia(CPEO)
美国耳鼻咽喉头颈外科学会	American Academy of Otolaryngology-Head and Neck Surgery(AAO-HNS)
美国食品与药品管理局	Food and Drug Administration(FDA)
蒙特利尔认知评价量表	Montreal Cognitive Assessment(MoCA)
脑干和脊髓受累并乳酸升高的白质脑病	leukoencephalopathy with brain stem and spinal cord involvement and lactate elevation(LBSL)
脑干听觉诱发电位	brain stem auditory-evoked potential(BAEP)
脑桥小脑角	cerebellopontine angle(CPA)
黏着斑激酶	focal adhesion kinase(FAK)
皮质基底节变性	corticobasal ganglionic degeneration(CBD)
氢质子磁共振波谱	hydrogen proton magnetic resonance spectroscopy(¹ H-MRS)
人工耳蜗植入	cochlear implantation(CI)
人工智能	artificial intelligence(AI)
β-人绒毛膜促性腺激素	β-human chorionic gonadotropin(β-hCG)
乳酸	lactic acid(Lac)
三叉神经诱发电位	trigeminal evoked potentials(BTEP)
上皮膜抗原	epithelial membrane antigen(EMA)
上皮样恶性外周神经鞘瘤	epithelioid malignant peripheral nerve sheath tumor (EMPNST)
上皮样肉瘤	epithelioid sarcoma(ES)
少突胶质细胞转录因子2	oligodendrocytes transcription factor-2(Olig-2)
神经微丝蛋白	neurofilament protein(NF)
神经元特异性烯醇化酶	neuron-specific enolase(NSE)
世界神经外科学会联合会	World Federation of Neurosurgical Societies(WFNS)
嗜铬素A	chromogranin A(CgA)
水痘-带状疱疹病毒	varicella-zoster virus(VZV)
丝裂原激活蛋白激酶/细胞外信号调节激酶	mitogen-activated protein kinase/extracellular signal-regulated kinase(MEK)
听觉脑干反应	auditory brain stem response(ABR)
听觉脑干植入	auditory brain stem implantation(ABI)
同源性磷酸酶-张力蛋白	phosphatase and tensin homologue(PTEN)
突触素	synaptophysin(Syn)
¹⁸ F-脱氧葡萄糖	¹⁸ F-fluoro-2-deoxy-D-glucose(¹⁸ F-FDG)
完全缓解	complete response(CR)