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颅内动脉瘤患者介入栓塞手术时机探讨及其预后的影响因素分析*

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摘要 目的:探讨颅内动脉瘤患者介入栓塞的手术时机及其预后的影响因素。**方法:**纳入安徽医科大学附属阜阳医院和安徽医科大学第一附属医院 2015 年 5 月~2017 年 5 月收治的颅内动脉瘤患者 130 例, 均行介入栓塞术治疗。根据手术时机分成早期组(n=78)、延期组(n=52)。早期组在发病≤3 d 行手术, 延期组在发病>3 d 行手术。比较两组术后动脉栓塞程度、并发症与 2 年内预后情况。根据预后分成良好组和不良组, 采用多因素 Logistic 回归分析患者预后的影响因素。**结果:**早期组完全栓塞率为 88.46%, 高于延期组的 73.08%, 差异有统计学意义($P<0.05$)。两组动脉瘤出血、肢体障碍、意识障碍、穿刺处感染、脑积水、电解质紊乱发生率比较无显著差异($P>0.05$)。早期组预后良好率为 79.49%, 显著高于延期组的 63.46%($P<0.05$)。不良组术前格拉斯哥预后评分(GOS)≤3 分、延迟期手术、瘤体位于后循环、高血压、糖尿病、Hunt-Hess 3~5 级、Fisher III~IV 级占比显著高于良好组($P<0.05$)。多因素 Logistic 回归分析结果提示术前 GOS 评分≤3 分、延迟期手术、瘤位置在后循环、高血压、糖尿病、Hunt-Hess 3~5 级、Fisher III~IV 级是患者预后的危险因素($P<0.05$)。**结论:**颅内动脉瘤患者早期行介入栓塞术, 能提高完全栓塞率, 改善预后, 患者预后不良主要与术前 GOS 评分、手术时机、瘤位置、高血压、糖尿病、Hunt-Hess 分级、Fisher 分级有关。

关键词:介入栓塞术; 颅内动脉瘤; 手术时机; 预后; 影响因素

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The Operative Time of Interventional Embolization and the Influencing Factors of Prognosis in Patients with Intracranial Aneurysm*

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ABSTRACT Objective: To explore the operative time of interventional embolization and the influencing factors of prognosis in patients with intracranial aneurysm. **Methods:** 130 patients with intracranial aneurysm who were admitted to Fuyang Hospital Affiliated to Anhui Medical University and the First Affiliated Hospital of Anhui Medical University from May 2015 to May 2017 were selected, they were treated with interventional embolization. The patients were divided into early group (n=78) and delayed group (n=52) according to the operative time. The early group was operated within 3 days after the onset of the disease, and the delayed group was operated after the onset of the disease>3 days. The degree of arterial embolism, complications and prognosis within 2 years were compared between the two groups. According to the prognosis, the patients were divided into the good group and the bad group. Multivariate logistic regression was used to analyze the influencing factors of patients' prognosis. **Results:** The complete embolism rate of early group was 88.46%, which was higher than 73.08% of delayed group, the difference was statistically significant ($P<0.05$). There were no significant differences between the two groups in the incidence of aneurysm hemorrhage, limb disorder, consciousness disorder, infection at puncture site, hydrocephalus and electrolyte disorder ($P>0.05$). The good prognosis rate of early group was 79.49%, which was significantly higher than 63.46% of delayed group ($P<0.05$). Bad group of preoperative Glasgow outcome scale (GOS)≤3 points, delay surgery, tumors located in the posterior circulation, hypertension, diabetes, Hunt-Hess grade 3~5, Fisher grade III~IV proportion were significantly higher than those of the good group ($P<0.05$). Multivariate logistic regression analysis showed that GOS score≤3 before operation, delayed operation, tumor location in the posterior circulation, hypertension, diabetes, hunt Hess grade 3-5, Fisher grade III-IV were the influencing factors of poor prognosis ($P<0.05$). **Conclusion:** Early interventional embolization can improve the complete embolization rate and prognosis of patients with intracranial aneurysm. The poor prognosis are mainly related to preoperative GOS score, operative time, tumor location, hypertension, diabetes, hunt Hess grade and Fisher grade.

Key word: Interventional embolization; Intracranial aneurysm; Operative time; Prognosis; Influence factor

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前言

颅内动脉瘤若未能及时治疗,则可能因动脉瘤破裂出血而导致死亡。研究表明这类患者预后欠佳,部分病例经治疗后存在神经功能缺损,且首次治疗后6个月内再出血率达30%~50%,复发率高^[1,2]。既往行传统开颅术,可将脑底池血液清除,预防脑血管痉挛,但该术式具有侵袭性,对颅脑造成损伤较大^[3]。近年来,血管内介入栓塞术在颅内动脉瘤治疗中体现出较多优势,如致残率低、死亡率低、侵袭性小等,其对改善患者病情意义重大^[4]。然而,临床针对介入栓塞术的手术时机存在争议,由于患者存在个体差异,部分病例因合并基础疾病等原因,导致手术时机不同,而不同手术时机对其疗效的影响可能也具有差异性^[5,6]。此外,研究表明介入栓塞术预后可能受到多种因素影响,但具体因素尚未明确^[7]。本研究纳入130例患者进行探讨,分析颅内动脉瘤患者介入栓塞手术时机及预后的影响因素,现报道如下。

1 资料与方法

1.1 一般资料

纳入安徽医科大学附属阜阳医院和安徽医科大学第一附属医院2015年5月~2017年5月收治的颅内动脉瘤患者130例,均行介入栓塞术治疗。根据手术时机分成早期组($n=78$)、延期组($n=52$)。早期组男41例,女37例,年龄49~83岁,平均(62.30 ± 8.89)岁。延期组男32例,女20例,年龄45~86岁,平均(63.43 ± 9.02)岁。两组性别、年龄比较无差异($P>0.05$)。

1.2 纳入与排除标准

1.2.1 纳入标准 (1)符合颅内动脉瘤诊断标准^[8]:临床表现为动眼神经麻痹、颅内压增高等,经头颅CT、脑血管数字造影、3D-CT血管造影可见局部血管壁受损,伴有异常膨出,证实为颅内动脉瘤,可见颅内血肿;(2)行介入栓塞术;(3)未见颅内占位性病变;(4)签署知情同意协议。

1.2.2 排除标准 (1)复发性动脉瘤;(2)既往有颅内手术史;(3)因外伤所致颅内血肿;(4)合并烟雾病、动静脉畸形等其他类型的脑血管病。

1.3 手术方法

早期组在发病 $\leq 3d$ 行手术,延期组在发病 $> 3d$ 行手术。术前行数字减影血管造影检查,明确动脉瘤部位、形态以及大小,实施全身麻醉。经Seldinger法于股动脉进行穿刺,留置导管。为了预防动脉内血栓发生,可给予全身肝素化治疗。根据瘤颈、瘤体大小,选取与之匹配的弹簧圈,将动脉瘤致密填塞,术后给

予抗脑血管痉挛、抗凝、抗血小板等治疗。

1.4 临床资料收集

收集患者的性别、年龄、瘤大小、术前GOS评分、手术时机、瘤位置、吸烟史、高血压、糖尿病、脑梗塞、高脂血症、Hunt-Hess分级、Fisher分级、手术方式、多发性动脉瘤、宽颈等临床资料。

1.5 观察指标与评价标准

(1)动脉栓塞程度评价^[9]:完全栓塞:栓塞范围为100%;大部分栓塞:栓塞范围为90%~99%;部分栓塞:栓塞范围 $< 90\%$ 。(2)并发症:分析两组动脉瘤出血、肢体障碍、意识障碍、穿刺处感染、脑积水、电解质紊乱的发生率。(3)术后随访2年,经格拉斯哥预后评分(Glasgow outcome scale, GOS)量表^[10]评估预后,死亡计1分,植物生存计2分,重度残疾计3分,轻度神经功能障碍计4分,基本无障碍计5分。其中1~3分为预后不良,4~5分为预后良好。(4)分级评估:① Hunt-Hess分级^[10]:1级:无明显症状,伴或不伴轻度头痛,2级:有明显头痛,存在动眼神经麻痹表现,颈强直;3级:轻微意识障碍;4级:处于偏瘫、半昏迷状态;5级:深度昏迷。② Fisher分级^[11]:I级:CT提示未见积血;II级:积血厚度不足1mm,未见血凝块形成;III级:积血厚度 $> 1mm$;IV级:脑室内有明显积血,或脑内血肿。

1.6 统计学方法

经SPSS24.0软件处理数据,计量资料以均数 $\pm$ 标准差($\bar{x}\pm s$)表示,行t检验。计数资料用(%)表示,行 χ^2 检验。多因素Logistic回归模型分析预后的影响因素。 $P<0.05$ 有统计学意义。

2 结果

2.1 两组栓塞程度比较

早期组完全栓塞率为88.46%(69/78),高于延期组的73.08%(38/52),延期组部分栓塞率为7.69%(4/52),高于早期组的0.00%(0/78),差异有统计学意义($P<0.05$),见表1。

2.2 两组并发症情况比较

两组动脉瘤出血、肢体障碍、意识障碍、穿刺处感染、脑积水、电解质紊乱的发生率比较无显著差异($P>0.05$),见表2。

2.3 两组2年内预后情况分析

早期组预后良好62例(79.49%),预后不良16例(20.51%)。延期组预后良好33例(63.46%),预后不良19例(36.54%),早期组预后良好率高于延期组($\chi^2=6.799, P=0.009$)。

2.4 影响患者预后的单因素分析

根据上述分析提示预后良好95例,预后不良35例,分别

表1 两组栓塞程度比较[n(%)]

Table 1 Comparison of embolism degree between two groups[n(%)]

Groups	n	Complete embolism	Most embolism	Partial embolism
Early group	78	69(88.46)	9(11.54)	0(0.00)
Delay group	52	38(73.08)	10(19.23)	4(7.69)
χ^2		5.071	1.479	3.880 ^①
P		0.024	0.224	0.049

Note: ① chi square test of continuity correction is adopted.

表 2 两组并发症情况比较[n(%)]

Table 2 Comparison of complications between the two groups[n(%)]

Groups	n	Aneurysm bleeding	Limb disorders	Disturbance of consciousness	Infection at puncture site	Hydrocephalus	Electrolyte disorder
Early group	78	1(1.28)	0(0.00)	0(0.00)	1(1.28)	0(0.00)	0(0.00)
Delay group	52	2(3.85)	3(5.77)	2(3.85)	2(3.85)	2(3.85)	3(5.77)
χ^2		0.128 [°]	2.403 [°]	1.037 [°]	0.128 [°]	1.037 [°]	2.403 [°]
<i>P</i>		0.721	0.121	0.309	0.721	0.309	0.121

Note: ° chi square test of continuity correction is adopted.

表 3 影响患者预后的单因素分析[n(%)]

Table 3 Single factor analysis on the prognosis of patients [n(%)]

Factors	n	Good group(n=95)	Bad group(n=35)	χ^2	<i>P</i>
Gender	Male	73	50(52.63)	1.778	0.182
	Female	57	45(47.37)		
Age	≥ 60 years old	69	48(50.53)	0.922	0.337
	< 60 years old	61	47(49.47)		
Tumor diameter	≥ 10 mm	43	33(34.74)	0.439	0.508
	<10 mm	87	62(65.26)		
Preoperative GOS score	> 3 points	58	52(54.74)	14.629	0.000
	≤ 3 points	72	43(45.26)		
Operative time	Early stage	78	62(65.26)	4.073	0.044
	Delay period	52	33(34.74)		
Tumor location	Anterior circulation	80	64(67.37)	5.067	0.024
	Posterior circulation	50	31(32.63)		
Smoking history	Yes	29	23(24.21)	0.737	0.391
	No	101	72(75.79)		
Hypertension	Yes	42	22(23.16)	13.508	0.000
	No	88	73(76.84)		
Diabetes	Yes	31	15(15.79)	12.613	0.000
	No	99	80(84.21)		
Cerebral infarction	Yes	16	12(12.63)	0.013 [°]	0.908
	No	114	83(87.37)		
Hyperlipidemia	Yes	20	15(15.79)	0.044	0.833
	No	110	80(84.21)		
Hunt-Hess grade	1~2	97	76(80.00)	5.401	0.020
	3~4	33	19(20.00)		
Fisher grade	I ~ II	89	71(74.74)	6.436	0.011
	III~IV	41	24(25.26)		
Operative methods	Balloon assisted	39	29(30.53)	1.413	0.493
	Stent assisted	38	30(31.58)		
	No assistance	53	36(37.89)		
Multiple aneurysm	Yes	32	24(25.26)	0.080	0.778
	No	98	71(74.74)		
Wide neck	Yes	31	22(23.16)	0.090	0.762
	No	99	73(76.84)		

Note: ° chi square test of continuity correction is adopted.

表 4 影响患者预后的多因素分析

Table 4 Multivariate analysis on the prognosis of patients

Variable	β	SE	Wald χ^2	P	OR	95%CI
Preoperative GOS ≤ 3 points	0.856	0.224	14.672	0.000	2.354	1.519~3.648
Delay period operation	0.664	0.329	4.069	0.044	1.942	1.019~3.701
Tumor in posterior circulation	0.686	0.308	4.964	0.026	1.985	1.086~3.628
Hypertension	1.211	0.329	13.566	0.000	3.356	1.762~6.392
Diabetes	1.407	0.406	12.010	0.000	4.085	1.843~9.054
Hunt-Hess 3~5 grade	1.133	0.481	5.534	0.019	3.104	1.208~7.976
Fisher III~IV grade	1.088	0.426	6.512	0.011	2.968	1.287~6.845

纳入良好组、不良组。不良组术前 GOS 评分 ≤ 3 分、延迟期手术、瘤位置在后循环、高血压、糖尿病、Hunt-Hess3~5级、Fisher III~IV级占比显著高于良好组($P<0.05$),见表3。

2.5 患者预后影响因素的多因素 Logistic 回归分析

将患者的预后情况作为因变量,表3中差异有统计学意义的指标作为自变量,多因素 Logistic 回归分析结果提示术前 GOS 评分 ≤ 3 分、延迟期手术、瘤位置在后循环、高血压、糖尿病、Hunt-Hess 分级3~5级、Fisher 分级III~IV级是患者预后的危险因素($P<0.05$),见表4。

3 讨论

颅内动脉瘤破裂出血的死亡率非常高,病情进展迅速。临床主张早期行手术治疗,降低死亡率。介入栓塞手术已被证实安全性高,针对动脉瘤血管予以栓塞处理,可预防再出血^[12]。然而,针对其手术时机,临床仍存在争议。研究指出在发病1周后行手术,死亡率约10%,然而,在发病2~3d内行手术,死亡率约5.3%^[13]。另有研究发现手术时机的差异可影响并发症发生率,从而影响疗效^[14]。本研究提示与延迟期行手术者比较,早期手术者完全栓塞率更高,且组间并发症发生率未见明显差异,也表明早期手术的疗效更显著,且安全性高,未增加并发症风险。

颅内动脉瘤患者介入栓塞术的预后是临床重点研究课题,部分患者行手术后,效果仍欠佳^[15]。临床需明确预后的影响因素,为制定治疗方案提供依据。我们通过分析患者预后的影响因素,提示术前 GOS 评分 ≤ 3 分、延迟期手术、瘤位置在后循环、高血压、糖尿病、Hunt-Hess 分级3~5级、Fisher 分级III~IV级是患者预后不良的影响因素。我们发现术前 GOS 评分 ≤ 3 分的患者预后更差。研究表明颅内动脉瘤患者因脑干受损,导致脑干功能下降,颅内压上升,瞳孔、意识、生命体征均发生变化,GOS 评分能对患者的意识障碍、语言障碍程度进行评估,是预测预后的重要指标^[16]。有学者发现 GOS 评分越低,提示预后越差,再出血风险增加^[17]。本组研究与上述结论基本吻合,也提示 GOS 评分与预后有关。本研究发现与早期手术者相比,延迟期患者的预后更差。研究表明在出血后72h内行手术,此时血液内白细胞并未彻底溶解,可预防血管痉挛,控制再出血风险^[18,19]。而在发病72h后行手术,血液凝块完全溶解,血红蛋白释放量增加,容易引起再出血^[20]。

我们发现与瘤体位于前循环相比,瘤体位于后循环者的预后更差。研究发现后循环瘤体较深,且瘤体类型大多比较复杂,

主要为大动脉、宽颈动脉瘤,病情较重,死亡率高,而前循环瘤体相对而言形态更规则,手术风险较低^[21,22]。因此,后循环瘤体疗效更差。在本研究中,合并高血压者的预后更差。在合并高血压的情况下,患者动脉壁存在明显粥样硬化,导致弹力纤维功能下降,增加了动脉壁压力,使营养血管处于闭塞状态,引起血管壁变性,可能诱发脑梗死、脑缺血,影响预后^[23,24]。

本研究提示与未合并糖尿病者相比,合并糖尿病者的预后更差。研究表明血糖与颅内动脉瘤患者意识状态、预后情况存在密切关联^[25]。糖尿病可引起脑血管变形,增加手术操作难度,延长手术时间,并且会增加脑栓塞发生的可能性^[26,27]。因此,临床医师在术前需对患者进行控糖治疗,每日对其血糖予以监测。我们发现 Hunt-Hess3~5级、FisherIII~IV级患者的预后较差。Hunt-Hess、Fisher 分级是评价动脉瘤破裂出血的重要标准,其分级越高,表明病情越重^[28]。有学者发现 Hunt-Hess、Fisher 分级越高的患者死亡率越高,容易出现脑积水、再出血等并发症,影响预后^[29,30]。这为本研究提供了依据,也进一步证实 Hunt-Hess、Fisher 分级与预后有关。

综上所述,与延迟期手术患者相比,早期行介入栓塞术,能提高完全栓塞率,改善预后,影响患者预后的因素包括术前 GOS 评分、手术时机、瘤位置、高血压、糖尿病、Hunt-Hess 分级、Fisher 分级,临床需引起重视。此外,本研究也有不足,如选取样本量少,未来还需扩大样本量予以探讨。

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