

不同年龄胆道闭锁患儿手术效果分析

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【摘要】 目的 分析胆道闭锁手术年龄与术后早期效果的关系以及较大年龄(>90 d)患儿的 Kasai 手术指征。**方法** 2004—2010 年复旦大学附属儿科医院收治胆道闭锁患儿 452 例,均经术中胆道造影确诊。手术采用标准的 Kasai 术,术后常规使用激素,对不同年龄组患儿术前肝功能、B 超等资料及术后胆红素下降情况进行分析,总胆红素水平低于 20 mmol/L 定为黄疸完全消退。**结果** 将所有患儿根据年龄分为三组,手术年龄 ≤ 60 d 者 146 例,手术年龄在 $60\sim 90$ d 者 222 例, >90 d 者 84 例($90\sim 100$ d 者 33 例, $100\sim 110$ d 26 例, $110\sim 120$ d 10 例, $120\sim 130$ d 8 例, >130 d 7 例)。术前各年龄组总胆红素、直接胆红素、谷丙转氨酶无显著差异。术后 2 周, 60 d 以内组,胆红素下降水平最低($P < 0.05$), <45 d 患儿胆红素下降水平并未更加显著。术后 3 个月随访率为 61.3% ,各年龄组总胆红素水平无显著差异($F = 0.132, P = 0.970$)。术后 6 个月随访率 37.4% , 90 d 以上组总胆红素(58.09 ± 58.55) mmol/L , 90 d 以内组总胆红素水平(27.67 ± 30.60) mmol/L ($P = 0.226$)。 >90 d 患儿,每间隔 10 d 分成一组,各组间术后早期胆红素下降水平无差异($F = 1.115, P = 0.355$)。 >90 d 手术患儿两年自体肝生存率为 36.1% 。 90 d 以上患儿延误手术原因: 39.2% 因家长未重视, 51.6% 因误诊婴儿肝炎耽误治疗。**结论** 胆道闭锁患儿 >90 d 并非手术绝对禁忌,多数患儿可取得较好的早期黄疸消退,部分患儿术后 6 个月可以有较好的肝功能恢复。

【关键词】 胆道闭锁; 外科手术; 治疗结果

The influence of age at surgery in patients with biliary atresia in older infants. CHEN Gong, ZHENG Shan, SUN Song, et al. Surgical Department of Children's Hospital of Fudan University, Shanghai 201102, China

【Abstract】 Objective To analysis the relationship between age and the early surgical outcome of Kasai procedure for the older infant with biliary atresia(BA). **Methods** All infants who had undergone surgery for BA during the period 2004 through 2010 were reviewed. During the study period, the definitive diagnosis was confirmed with operative cholangiogram and the details of liver function before and after the operation were reviewed. **Results** A total of 452 infants have type III BA diagnosis during this period. All of the patients were divided into 3 groups according to their age at operation (group A: on or before 60 days (146 cases); group B: between 60 to 90 days (222 cases); group C: on or after 90 days (84 cases). The total bilirubin level (TBIL), direct bilirubin level (DBIL), and alanine transaminase (ALT) level showed no difference between each group before the Kasai procedure. The worst outcome of clearance of jaundice was found in group A, but not in group C two weeks postoperatively ($P < 0.05$). In the point of three months and six month postoperative, TBIL in each group showed no difference. In group C, two year survival rates of our patients with their native livers were 36.1% . **Conclusion** Perform the Kasai operation beyond the age of 90 days was not associated with a worse outcome. A part of patients could still achieve good bile flow with normal bilirubin postoperatively.

【Key words】 Biliary Atresia; Surgical Procedures, Operative; Treatment Outcome

Kasai 手术是胆道闭锁唯一有效的治疗方法和移植过渡手段。2009 年 Shinkai 报道了 80 例胆道

闭锁患儿,Kasai 术后 20 年自体肝存活率可达到 44% ^[1]。对预后不佳患儿有学者主张可直接接受肝移植手术。然而,究竟什么因素能提示患儿预后? 众多文献认为年龄是关键因素^[2,3]。但 2010 年 Wong 等观察 103 例患儿术后 1 年的生存及退黄情

况,发现并不存在 60 d 这个以往认为是预后好坏的分界^[4]。Davenport 回顾了年龄 > 100 d 患儿手术效果,发现这些患儿 2 年自体肝生存率约 40%,并不比小年龄组低^[5]。目前国内胆道闭锁手术年龄多控制在 90 d 以内,究竟年龄是不是决定患儿预后的因素,大年龄组患儿手术效果如何,是否病理评分能给预后一个明确的提示,是本文探讨的问题。

材料和方法

一、研究对象及分组

2004—2010 年复旦大学附属儿科医院收治胆道闭锁患儿 519 例,所有病例均行术中胆道造影明确诊断,其中放弃 Kasai 手术 38 例,排除手术证实 I 型胆道闭锁 29 例,其余 452 例均为 III 型胆道闭锁。手术年龄 < 60 d 患儿 146 例(A 组);手术年龄 60 ~ 90 d 者 222 例(B 组);≥90 d 84 例(C 组,其中 90 ~ 100 d 者,33 例,100 ~ 110 d 26 例,110 ~ 120 d 10 例,120 ~ 130 d 8 例,> 130 d 7 例)。

年龄 90 d 以上病例中,来本院首诊 111 例,入院后经胆道造影未接受根治手术的患儿 27 例,平均年龄为(120.7 ± 21.48)d,接受 Kasai 术组 84 例,平均年龄为(106.69 ± 16.16)d。

二、治疗方案

手术采用标准的 Kasai 术,切除肝门纤维块,Roux-en-Y 肝门空肠吻合,空肠袢肝支长度 35 ~ 50 cm,术后第 5 天常规静脉滴注甲基强的松龙 4 mg · kg⁻¹ · d⁻¹,每 3 天根据黄疸消退情况递减或再次原剂量激素冲击 3 d。黄疸消退不明显,则长期口服甲基强的松龙 2 mg · kg⁻¹ · d⁻¹,再根据黄疸消退缓慢递减。术后患儿静脉用头孢曲松钠或亚

胺培南 1 个月,继续口服抗生素两药交替至 6 个月。总胆红素水平低于 20 mmol/L 定为黄疸完全消退。

三、观测指标

对不同年龄三组患儿术前总胆红素、直接胆红素、转氨酶水平;术后 2 周总胆红素及胆红素下降比例(术前总红素 - 术后总胆红素)/术前总胆红素;术后 3 个月、6 个月三组患儿总胆红素水平进行回顾分析。

四、统计分析

多组间均数比较采用单因素 ANOVA 方差分析,两组比较采用两独立样本 *t* 检验。统计分析采用 SPSS 17.0 软件,*P* < 0.05 为差异有统计学意义。

结果

一、90 d 以上患儿延误治疗原因

90 d 以上患儿延误手术原因:39.2% 因家长辗转多家医院延误病情,51.6% 因当作婴儿肝炎拖延了治疗。90 d 以上入院未行手术的患儿(27 例)平均年龄(120.7 ± 21.48)d,手术组(84 例)平均年龄(106.69 ± 16.16)d,该两组比较 *P* = 0.004。放弃手术 27 例患儿中,15 例是家长因负面信息或个人原因放弃治疗;7 例因为肝脏过大,肝门暴露困难,医生术中放弃;5 例合并严重心脏等畸形。

二、各年龄组术前总胆红素、直接胆红素、谷丙转氨酶水平

术前血清总胆红素水平三组无显著差异(*F* = 1.279, *P* = 0.279);直接胆红素:A 组(< 60 d 组)较高,但与 B 组(60 ~ 90 d 组)及 C 组(90 d 以上手术组)无显著差异(*F* = 2.917, *P* = 0.055);术前转氨酶水平也未见差异(*F* = 2.84, *P* = 0.059,见表 1)。

表 1 术前各年龄组总胆红素、直接胆红素、谷丙转氨酶水平比较($\bar{x} \pm s$)

Table 1 Each age group total bilirubin, direct bilirubin, alanine aminotransferase levels of preoperative($\bar{x} \pm s$)			
分组	总胆红素 (mmol/L)	直接胆红素 (mmol/L)	转氨酶 (U/L)
60 d 组	179.52 ± 59.77	178.86 ± 59.76	95.29 ± 71.31
60 ~ 90 d 组	172.10 ± 54.74	171.24 ± 50.75	127.71 ± 179.88
90 d 组	164.98 ± 64.93	160.48 ± 61.55	113.51 ± 63.05

注:术前三组总胆红素,直接胆红素,ALT 水平无显著差异。

三、各年龄组术后 2 周胆红素水平、下降比例及术后 3 个月总胆红素水平

术后 2 周总胆红素水平,手术年龄 ≤ 60 d 组为(124.96 ± 55.87) mmol/L,较术前下降(27 ± 2.5)%;60 ~ 90 d 手术组为(103.69 ± 42.08) mmol/L,较术前下降(37.9 ± 1.5)%;> 90 d 手术组为

(92.17 ± 56.35) mmol/L,较术前下降(41.8 ± 2.8)%。其中 < 60 d 组术后 2 周总胆红素水平较 60 ~ 90 d 组及 90 d 以上组要高(*F* = 3.39, *P* = 0.018 < 0.05),下降比例偏低(*F* = 10.55, *P* = 0.00 < 0.01),而后两组该值无显著差异(*P* = 0.236 > 0.05)(图 1)。将 > 90 d 手术患儿,每间隔 10 d 分

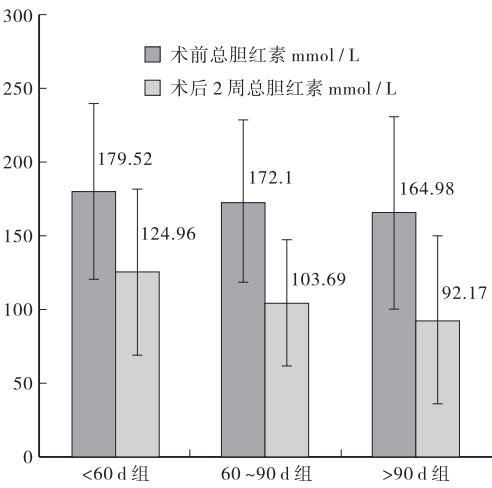


图 1 术前及术后 2 周三组总胆红素数值, 60 d 组术后 2 周总胆红素水平较高 ($F = 3.39, P = 0.018 < 0.05$), 下降比例偏低 ($F = 10.55, P = 0.00 < 0.01$)。

Figure 1 Preoperative and postoperative 2 weeks three groups total bilirubin values, postoperative group B after two weeks total bilirubin level is higher ($F = 3.39, P = 0.018 < 0.05$), Drop ratio is low ($F = 10.55, P = 0.00 < 0.01$)。

表 2 90 d 以上各年龄段术前及术后 2 周胆红素比较

Table 2 All age groups of more than 90 days preoperative and postoperative bilirubin 2 weeks compared

手术年龄	术前总胆红素	术后 2 周总胆红素	胆红素下降比例
90 ~ 100 d	152.84 ± 41.74	80.39 ± 40.60	47.4 ± 3.8%
100 ~ 110 d	174.7 ± 78.92	95.18 ± 54.80	43.4 ± 4.2%
110 ~ 120 d	150.29 ± 45.07	107.08 ± 56.47	27.0 ± 11.6%
120 ~ 130 d	159.73 ± 83.71	108.33 ± 111.65	40.0 ± 9.9%
130 d ~	159.41 ± 67.26	93.0 ± 38.93	36.1 ± 9.3%

注: 90 d 以上各年龄段术前术后 2 周胆红素水平及下降比例无显著差异。

讨论

2008 年 Marie-Odile Serinet 报道一组 695 例接受手术患儿, 从 30 d 开始至 90 d, 每隔 15 d 分一组, 自体肝长期生存率呈逐步下降趋势^[2]。Sharad I. Wadhwani 等分析 55 例患儿, 预后较差组平均手术年龄为 72 d, 而预后较好组的平均手术年龄为 52 d^[3]。因此, 众多学者认为接受 Kasai 手术的患儿年龄越大, 术后退黄效果越差。Wong 等在众多决定预后的因素中, 对年龄进行专门研究, 发现相当一部分 >60 d 患儿可以取得良好的手术效果, 而且到 100 d 为止, 年龄并未对预后造成重要影响^[4]。Davenport 报道的手术年龄 > 100 d 患儿 (平均 133 d) 5 年自体肝生存率仍可达 45%^[5]。本组病例回顾认为, 术后 6 个月, 90 d 以内接受手术两组患儿虽然黄疸参数较 >90 d 手术患儿略低, 但三组并

成一组, 术前总胆红素水平无显著差异 ($F = 0.534, P = 0.711 > 0.05$), 各组术后 2 周胆红素下降比例亦无显著差异 ($F = 1.466, P = 0.221 > 0.05$) (表 2)。

术后 3 个月随访率为 81.0%, 60 d 以内组总胆红素水平为 (39.33 ± 17.76) mmol/L, 60 ~ 90 d 组为 (39.01 ± 23.09) mmol/L, > 90 d 组为 (38.2 ± 21.81) mmol/L, 各组无显著差异 ($F = 0.013, P = 0.987 > 0.05$)。

四、术后 6 个月总胆红素水平

术后 6 个月随访率为 64.3%, 总胆红素水平: 60 d 以内组为 (32.76 ± 38.97) mmol/L, 60 ~ 90 d 组为 (29.59 ± 35.51) mmol/L, 90 d 以上组总胆红素 (58.09 ± 58.55) mmol/L, 三组数值无显著差异 ($F = 1.188, P = 0.32 > 0.05$)。术后 6 个月接受随访的手术年龄在 90 d 以上患儿黄疸完全消退 33 (39.2%) 例, 术后两年 90 d 以上手术患儿自体肝生存率为 36.1%, 随访率为 51.2%。

无显著差异, 很多年龄较大患儿也可取得较好的术后早期退黄率。因此仅按照年龄大小决定放弃 Kasai 手术是武断的^[5]。

对于大年龄组患儿, 究竟有无手术年龄的上限? Schoen 报道一组 31 例患儿, 手术年龄最大 120 d, 术后也有很好的退黄率^[8]。2001 年 Chardot 报道了年龄最大年龄 141 d 患儿, 取得手术成功^[9]。Davenport 报道的最大手术年龄是 180 d^[5], 而日本 30 年回顾分析中报道的最大手术年龄为 421 d。本组病例中有 7 例年龄 > 130 d, 年龄最大 179 d, 3 例术后取得良好效果。因此, 手术年龄可不设置绝对上限。本组一些大年龄患儿不手术有以下原因: ①肝脏较大, 妨碍肝门部显露, 胆肠吻合手术难度加大。②多数医生观念中对手术年龄存在限制。③家长不愿意手术。

本研究发现 60 d 以内手术患儿, 术后早期退黄最差。1999 年 Karrer 等也有类似报道^[6]。对于这

一问题的解释,有人提出胆道闭锁可能是一组疾病的共同表现,畸形与感染因素共存,患儿发病年龄越小则以畸形为主,较大患儿则以围产期感染为主^[7]。大年龄患儿由于病变时间偏长,畸形因素相对较轻,上游胆汁淤积重,术后较大的压力差导致胆红素短期内排泄快,故早期黄疸消退更明显。

既然年龄不是影响手术预后的唯一因素,那么究竟何种因素对患儿预后有更为直接的决定作用?1997 年 Azarow KS 等从病理学角度对 33 例患儿预后相关因素进行分析认为:病理发现多形巨细胞、肝小叶间感染、局灶坏死、桥接坏死、胆管炎提示预后不良,而肝小叶中央区域有胆汁淤积是预后较好的标志^[10]。此外,也有学者通过术中经过脐静脉测量门脉压力,觉得这一参数能准确预测患儿最终发生门脉高压大出血的可能,压力大于 15 cmH₂O 则预后不佳^[11]。还有人通过 B 超测定肝硬化程度、肝脏大小,术后退黄情况以及血浆透明质酸水平等作为判断预后的参数。当然这些都还存在着争议^[12]。是否有某种单一因素或参数能精确预测预后,还是多个参数按不同权重才决定预后,还需更深入研究。

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