

·综述 General review·

第一代 Matrix 可吸收聚合物弹簧圈治疗颅内动脉瘤的研制及应用现状

吴 曦, 刘建民

【摘要】 目前颅内动脉瘤治疗的首选方法为介入治疗,但介入治疗同开颅治疗一样有一定的复发风险,且复发后严重威胁患者生命及生活质量。本文细述了第一代 Matrix 可吸收聚合物弹簧圈的研制理念及作用机制,并比较了其临床多中心治疗颅内动脉瘤的临床结果。

【关键词】 Matrix 弹簧圈;可吸收聚合物弹簧圈;颅内动脉瘤

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The present development and status of the first generation of Matrix bioabsorbable poly-meric material coil in the treatment of intracranial aneurysms WU Xi, LIU Jian-min. Department of Neurosurgery, Changhai Hospital, the Second Military Medical University, Shanghai 200433, China

【Abstract】 Endovascular coil embolization is the first primary technique of choice for treating intracranial aneurysms in many centers around the world, but some patients still got recanalizations months later, that may lead to death or severe disability just as the same in neurosurgery. This review showed the technic details of the first generation of Matrix bioabsorbable poly-meric material coil, and analyzed clinical results among many treatment centers, involving the therapeutic measure of intracranial aneurysms. (J Intervent Radiol, 2008, 17; 828-830)

【Key words】 Matrix coil; Bioabsorbable poly-meric material coil; Intracranial aneurysms

第一代 Matrix 可脱弹簧圈(简称 Matrix)是第一代具有生物活性涂层的弹簧圈,其设计初衷是为了增强机体对弹簧圈的炎性反应(生物活性反应),促进动脉瘤的机化和收缩,从而可不必致密栓塞,并可减轻动脉瘤变形、移位,减少动脉瘤体积引起的占位效应,减少动脉瘤复发比率。然而临床随访结果却与之稍有出入。

1 弹簧圈的组成

Matrix 是 Boston Scientific 公司生产并投入临床应用的生物可吸收聚合物弹簧圈(bioabsorbable poly-meric material coil. BPM/GDC),内核由铂金弹簧圈构成,占总体积的 30%,其外层占 70%,由生物活性涂层覆盖,其中 90%为聚羟乙酸,10%为聚丙烯酸。此涂层聚合物含量比例的设计,来自于使用不同比例涂层,栓塞猪动脉瘤模型的随访结果。发现聚羟乙酸/聚丙烯酸为 9:1 的涂层,生物相容性

较好,能尽可能避免引起过强的炎症反应而造成载瘤动脉的狭窄、闭塞或血栓形成,并可在 90 d 内被完全分解吸收,最符合 GDC 弹簧圈栓塞动脉瘤的自然病程^[1-3]。弹簧圈最外层还有亲水膜,在水中可减少摩擦力。

2 动物实验结果

虽然体外培养未见内皮细胞于 polyglycolic/polylactic acid 涂层繁殖^[4]。但对 24 枚猪颈总动脉侧壁型动脉瘤进行的随机对照试验显示,即使治疗时动脉瘤未达致密栓塞,2 周后 Matrix 组动脉瘤仍显示出致密栓塞,3 个月后所有 Matrix 组动脉瘤均缩小,且无载瘤动脉狭窄闭塞现象^[5]。可以说短期的动物试验随访结果很令人鼓舞。对 52 只猪进行相似研究的组织学检查显示,在术后 14 d 和 3 个月时,Matrix 组动脉瘤瘤颈组织覆盖物的厚度均明显大于 GDC 组动脉瘤,组织反应主要以中性粒细胞和机化良好的肉芽组织为主。但是 6 个月时两组瘤颈组织覆盖厚度却无明显差异^[6]。相似的组织反应性在新西兰兔弹力层诱导模型上也可观察到,Matrix 组动

作者单位:200433 上海 第二军医大学长海医院神经外科

通讯作者:刘建民

脉瘤的组织炎症反应性比 Hydro-coil 组和 GDC 组都强烈,并可观察到 Matrix 弹簧圈组动脉瘤比 GDC 组动脉瘤有更厚的瘤颈组织覆盖,但于 2、6、10 周为时间点的造影随访并没有发现 Matrix 弹簧圈组与 GDC 组、Hydro-coil 组的区别。该试验研究者认为,如果仅有生物活性反应,而无机械稳定性,可能无法减少 Matrix 弹簧圈组动脉瘤复发率,临床根据造影结果判断复发,而不在乎是否有组织反应^[7]。众所周知,复发患者的再出血率(7.9%)比造影稳定患者(0.4%)要高很多^[8]。所以弹簧圈仅有组织反应性是不够的,其最终目的是尽可能降低动脉瘤栓塞后长期的复发率。

对犬的大型宽颈分叉部动脉瘤于 2 周和 3 个月时的造影及组织学结果显示,Matrix 弹簧圈组比 GDC 组动脉瘤内产生更多的纤维结缔组织。但是对于大型分叉部动脉瘤,Matrix 弹簧圈并没有减少复发的发生率(2 周时 50%复发,3 个月时 67%复发)^[9]。这与以往 GDC 相似方式试验的复发率没有明显差别(2 周内 2/3 发生复发,3 个月进一步加重复发)^[10]。研究者认为 Matrix 弹簧圈可能比 GDC 对动脉瘤栓塞效果更差,它虽然表现出了更强的组织反应性,但是治疗大型分叉部动脉瘤,即使致密栓塞,复发率仍很高。上述试验提示血流动力学对于 Matrix 弹簧圈栓塞后的动脉瘤预后意义更大。

3 临床应用结果

对于 Matrix 弹簧圈的涂层在人体中是否具有炎症反应性,组织工程学已经有了多年的临床证据。但是关于 Matrix 弹簧圈作用于人体颅内动脉瘤的直接证据还比较少。Szikora 等^[11]对 18 例进行栓塞治疗且复发的动脉瘤进行病理检查,其中 2 例使用了 Matrix 弹簧圈。1 例致密栓塞,随访时间达 6 个月,另 1 例为术后 8 d。对于术后 8 d 的 Matrix 和 3 个月的 GDC 进行的病理检查未见明显区别。而随访 6 个月的 Matrix 栓塞动脉瘤的外观为微黄色,与 GDC 不同。该动脉瘤中完全由具有活性的成纤维细胞组成的肉芽组织充填,没有血栓和空腔残留。在另外 3 例使用 GDC 弹簧圈 3 年后切除的样本中,动脉瘤囊绝大部分由机化的血栓堵塞,但是仍有部分残腔留有未机化血栓和新鲜血液。此结果显示出了 Matrix 弹簧圈与 GDC 圈在人体内的组织学区别,证明了 Matrix 弹簧圈的涂层确实可以引起炎症反应并促进血栓机化的设计理念。

荟萃分析 2007 年 11 月前文献,经 Matrix 弹簧

圈治疗的 1477 例动脉瘤,平均随访时间 3 ~ 12 个月。从手术并发症率来看,除少数学者认为 Matrix 弹簧圈比 GDC 多 20% 的栓塞风险外^[12],大部分学者认为 Matrix 弹簧圈并不比 GDCs 圈的并发症率高。有学者认为 Matrix 的摩擦力较大,降低了其致密栓塞动脉瘤的可能性^[13]。而栓塞的致密度,很可能严重影响动脉瘤的长期预后^[14]。上述 1477 例动脉瘤的总并发症率为 10.94%,与弹簧圈相关的并发症中,血栓的发生率最高,占有所有并发症的 46.15%,而术中动脉瘤再次破裂出血占有所有并发症的 23.08%。这一结果包括了很多学者认为 Matrix 可能不必致密栓塞,从而适当降低了动脉瘤的术中破裂率,也包括了弹簧圈较硬,增加了动脉瘤术中的破裂率,但是总体来说,动脉瘤的术中破裂率没有明显高于 GDCs 圈。

Matrix 弹簧圈在使用的安全性上与 GDC 并无明显差异,其治疗的长期预后将更值得我们关注。诸多学者认为 Matrix 不能减少动脉瘤栓塞后的复发率^[15-17]。上述 1447 个动脉瘤的各组复发率从 19.5% 至 41%^[18,19]。而 Niimi 等^[20]将复发定义为动脉瘤显影增加超过 10%,发现该组 Matrix 弹簧圈栓塞的动脉瘤复发率为 57.4%,并认为 Matrix 弹簧圈治疗的大型动脉瘤复发率非常高,可达 82%,其长期预后可能不如 GDC。鉴于该研究中 74 例动脉瘤的即刻完全栓塞为 17%,瘤颈残留和不全栓塞率分别达 41% 和 42%,不全栓塞的比例非常高,并且该组病例中大型动脉瘤比例较高(11 例)。如此高的复发率可能与动脉瘤的栓塞致密度较低以及大型动脉瘤比例较高有关。相对而言,GDC 的长期栓塞复发率为 13% ~ 34%^[21-23],比 Matrix 弹簧圈稍低,而且上述 Matrix 弹簧圈的随访结果多为中期随访,对于其长期疗效尚无法肯定。Pierot 等^[24]多中心 Matrix 弹簧圈治疗颅内动脉瘤后长期随访的结果却认为 Matrix 弹簧圈效果很好。平均(14 ± 4)个月的随访发现动脉瘤的复发率达 25.7%,认为 Matrix 弹簧圈不能减少动脉瘤复发率。这也再次提示 Matrix 弹簧圈涂层吸收后动脉瘤内血液流变学改变对动脉瘤复发可能负主要责任。但是他们发现动脉瘤进一步栓塞率达 30%,说明 Matrix 确实增强了生物反应性。

众所周知,支架辅助 GDCs 圈治疗动脉瘤取得了良好的长期预后,有学者报道他们使用 Neuroform 支架辅助 Matrix 弹簧圈治疗小型动脉瘤方面的经验,认为比单用 Matrix 弹簧圈复发率更低^[25]。更进一步的证据还需要大样本的观察,而且对于 Matrix


弹簧圈结合支架治疗大型、宽颈或是分叉部的动脉瘤的疗效尚缺乏证据,而这些恰恰正是颅内动脉瘤治疗需要克服的难点。

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作者: 吴曦, 刘建民, WU Xi, LIU Jian-min
作者单位: 第二军医大学长海医院神经外科, 上海, 200433
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