

· 综 述 ·

血栓弹力图在颅内动脉瘤支架辅助栓塞术后抗血小板治疗中的应用进展

张一川 综述 柴尔青 审校

【关键词】 颅内动脉瘤; 支架; 血管内栓塞; 血栓弹力图; 抗血小板治疗

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普通人群颅内动脉瘤的发病率约为3%,一旦破裂,病死率、致残率较高^[1-4]。近年来,支架辅助弹簧圈栓塞被广泛报道用于治疗颅内动脉瘤^[5,6],但术后需要长期应用双重抗血小板药物治疗^[7,8]。受基因多态性等因素的影响,抗血小板药物的疗效具有极强的个体差异性。血栓弹力图(thromboelastography, TEG)是一种测量血栓形成和溶解动力学的方法,可提供凝血和纤溶状态的全面实时分析^[9],可用来评估血小板反应性和抗血小板药物的效果^[10]。本文就 TEG 在颅内动脉瘤支架辅助栓塞术后抗血小板治疗中的应用进展进行综述,为临床提供参考。

1 TEG 概述

1948 年, Hartert 发明了一种方法,用以测量血栓形成和溶解的动力学特征,可提供凝血和纤溶状态的全面实时分析,并命名为 TEG^[11]。TEG 利用高岭土或组织因子对全血进行处理,让机器自动监测血栓形成及溶解过程,产生多个不同参数,其中常用的参数包括 R 值、K 值、 α 角和最大幅度(maximal amplitude, MA)^[12]。阿司匹林通过花生四烯酸(arachidonic acid, AA)途径发挥抗血小板作用,而氯吡格雷通过二磷酸腺苷(adenosine diphosphate, ADP)途径发挥作用^[13]。AA 抑制率和 ADP 抑制率两指标可用来反应阿司匹林和氯吡格雷抗血小板的疗效,同时氯吡格雷的药物疗效也可以用 MA-ADP 来反映^[14]。在 MA-ADP 正常范围外,其数值越高,说明对氯吡格雷的反应越差,药物疗效也越差^[15]。但

TEG 也具弊端,如尚无法完全模拟机体凝血状况,因实验是在恒温下进行,尚不能监测体温改变是否会对结果产生影响。

2 TEG 参数同缺血与出血风险的关系

TEG 参数具有很强的临床应用价值,各参数不仅反映凝血因子、血小板功能,同时也反映抗血小板药物的疗效。TEG 参数 R 值增高、MA-ADP 降低与颅内动脉瘤支架辅助栓塞术后出血事件相关,而且 R 值>7.6 min、MA-ADP<29.2 mm 预测出血事件的 ROC 曲线下面积分别为 0.76(95%CI 0.70~0.82)和 0.89(95%CI 0.86~0.93)^[16];AA 抑制率和 ADP 抑制率增高提示术后发生出血事件的风险明显增加^[17,18]。TEG 参数 R 值预测缺血性卒中中支架置入术后出血事件的 ROC 曲线下面积为 0.817(95%CI 0.746~0.887)^[19]。

TEG 检测 ADP 抑制率降低、MA-ADP 升高与颅内动脉瘤支架辅助栓塞术后缺血事件相关^[20-22],MA-ADP 预测缺血事件的 ROC 曲线下面积为 0.67(95%CI 0.57~0.81; $P<0.05$)^[20]。TEG 监测 α 角增大与颅内动脉瘤血流导向装置置入术后缺血性事件有关^[23]。

这些研究指出了与缺血事件或出血事件可能相关的参数,但其参数标准并未统一。需要进一步开展与 TEG 相关的大型临床研究来进一步证实其相关关系,并统一相关参数标准。

3 TEG 参数与颅内动脉瘤介入术后抗血小板方案制定的关系

颅内动脉瘤支架辅助栓塞术后使用常规双抗治疗通常并不安全可靠,血栓事件是主要的并发症。Ryu 等^[24]研究表明颅内破裂动脉瘤支架辅助栓塞术后接受常规双抗治疗发生出血概率较高。Choi 等^[25]研究显示颅内动脉瘤支架辅助栓塞术后血栓事件发

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作者单位:750004 银川,宁夏医科大学临床医学院(张一川);730000 兰州,甘肃省人民医院脑血管病中心/甘肃省脑血管病重点实验室(张一川、柴尔青)

通讯作者:柴尔青, E-mail: happybirds998@162.com

生率约为25.5%，而单纯弹簧圈栓塞术后血栓事件的发生率约为12.4%。因此，制定个体化的抗血小板方案迫在眉睫，尤其是颅内破裂动脉瘤支架辅助栓塞术后的病人。

TEG参数反映血小板功能及抗血小板药物的疗效，根据TEG参数制定个体化的抗血小板治疗方案有助于提高抗血小板药物疗效，减少术后出血、缺血并发症^[24-28]。Li等^[26]根据TEG监测AA抑制率、ADP抑制率和MA-ADP值决定颅内破裂动脉瘤支架辅助栓塞术后抗血小板药物的具体剂量，AA抑制率、ADP抑制率越高，抗血小板药物用量越低；MA-ADP值越低，抗血小板药物用量越少；如果有出血或缺血症状，则增加或减少抗血小板药物的剂量；如果没有出血或缺血症状，则维持6个月；结果显示，这种抗血小板治疗方案明显减少术后出血、缺血事件。McTaggart等^[27]研究显示，根据TEG监测ADP抑制率调整抗血小板用药方案有助于控制出血事件发生率，然而氯吡格雷抵抗病人增加抗血小板药物剂量并不能彻底消除血栓事件，原因是调整药物剂量幅度并不能满足术后抗血小板治疗的要求，亦或是药物严重抵抗病人不仅仅是调整药物可能需要更换药物种类。张亮等^[28]研究显示，颅内动脉瘤支架辅助栓塞术后根据TEG调整抗血小板方案更安全。

总之，TEG是方便快捷、参数准确的一种检测手段，可以快速评价病人血小板功能。同时，依据TEG参数制定个体化抗血小板方案相对更安全。TEG参数可以作为颅内动脉瘤支架辅助栓塞术后个体化抗血小板治疗方案的依据，降低不良事件概率，为病人获得更加良好预后提供保障。由于相关研究仍较少，需要进一步临床研究。

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