Research progress in drug-coated balloon or/and directional atherectomy in treatment of complex femoropopliteal artery lesions

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[**Abstract**] Complex femoropopliteal artery lesions (CFPAL) is a clinical difficulty. Dug-coated balloon (DCB) can carry the drug directly to the lesion site for release, so that the drug can accumulate at the target site in a high concentration and inhibit intimal hyperplasia. Directional atherectomy (DA) can make the drug carried by DCB penetrate into the vascular wall better by removing the vascular plaque, and improve the clinical therapeutic effect. The application advances of DCB or/and DA in treatment of CFPAL were reviewed in this paper.

[**Keywords**] peripheral arterial disease; lower extremity; femoral artery; popliteal artery; arteriosclerosis obliterans; balloon; transluminal extraction-atherectomy therapy

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药物涂层球囊及定向斑块旋切术治疗复杂股腘动脉病变研究进展

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[**摘 要**] 复杂股腘动脉病变(CFPAL)是临床治疗难点。药物涂层球囊(DCB)可携带药物直达病变部位释放,使药物在靶部位高浓度聚集,且可抑制内膜增生。定向斑块旋切术(DA)可通过切除血管斑块使 DCB 携带的药物更好地渗透入血管壁,提高临床治疗效果。本文对 DCB、DA 治疗 CFPAL 的应用进展进行综述。

[**关键词**] 外周血管疾病;下肢;股动脉;腘动脉;闭塞性动脉硬化;球囊;血管腔内斑块旋切术

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动脉硬化闭塞症(arteriosclerosis obliterans, ASO)是一种全身性疾病,主要累及大、中动脉,当病变累及腹主动脉下段及其远端主干动脉时,可引起下肢急性或慢性缺血。随着镍钛合金支架的出现[1],血管腔内治疗逐渐成为下肢 ASO 临床首选血运重建方法;但术后血管或支架内再狭窄(in-stent restenosis, ISR)仍是困扰临床医师的主要问题,特别是复杂和特殊部位病变,如膝关节区,由于运动导致血管内产生持续外压,可致 ISR、支架断裂和闭塞发生率增加[2]。药物涂层球囊(drug-coated balloon, DCB)可携带药物直达病变部位释放,同时抑制内膜增生。定向斑块旋切术(directional atherectomy, DA)可以通过切除血管斑块使 DCB 携带的药物更好地渗透入血管壁发挥临床治疗效果。DCB 联合 DA 可显著改善血管腔内治疗 ASO 1 年后靶血管通畅率[3-5]。本文对 DCB 和/或 DA 治疗复杂股腘动脉病变(complex

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femoropopliteal artery lesions, CFPAL)的研究进展进行综述。

1 CFPAL

2007 年第 2 版泛大西洋国际共识(Transatlantic Inter-Society Consensus, TASC Ⅱ)根据血管病变复杂程度将股腘动脉病变分为 A～D 型;其中 C 型和 D 型具有病变血管长、直径细、弥漫性钙化和多发血管性疾病等特点,加之部分患者伴有基础疾病(如糖尿病),发生二次狭窄、再闭塞和急性血栓形成等风险高[6-7],并将此类下肢血管病变定义为 CFPAL。有效治疗 CFPAL 是临床难点[5]。我国 2016 版《下肢动脉硬化闭塞症诊治指南》推荐对 TASC Ⅱ A～C 型股腘动脉病变首选腔内治疗,TASC Ⅱ D 型合并严重内科疾病或存在其他手术禁忌时也可选择腔内治疗[8-9]。既往研究[10-11]结果显示,单纯经皮腔内血管成形术(percutaneous transluminal angioplasty, PTA)或支架治疗 CFPAL 成功率较高,但远期通畅率不满意。近年来,DCB 扩张术已成为治疗股腘动脉疾病的重要手段,相比单纯 PTA 治疗 CFPAL 更具优势。既往研究[12-14]表明,DCB 联合 DA 可有效降低长段靶病变血管重建率(target lesion revascularization, TLR)。

2 DA 与 DCB

目前国内多使用 SilverHawk 及 TurboHawk 斑块旋切系统,均为美国 ev3 公司产品,后者属于更新型,切割效率更高,适用于钙化较为严重的病变血管斑块。旋切系统主要由切割导管部分和驱动部分组成;为避免发生远端栓塞,可使用保护伞装置,其锥形头端可辅助扩张远端管腔并压迫斑块。该装置可有针对性地去除动脉粥样硬化斑块,并尽可能保留正常血管结构,缺点是需多次重复才能消除一定体积的斑块。Pantheris 动脉斑块切除装置(美国 Avinger 公司)是最近获得美国食品药品监督管理局批准的新型 DA 装置。Pantheris 导管配备光学相干断层成像(optical coherence tomography, OCT)装置,可在无电离辐射的情况下直接使动脉腔可视化,确保导管更安全、快速地到达病变血管部位,更有针对性地去除偏心斑块,增加旋切术的疗效和安全性,同时最大限度地降低非病变血管壁损伤风险,适用于治疗直径为 3～7 mm 的血管。此外,由 OCT 获取的数据可进行血管 3D 图像重建,使术者更好地观察病变部位,减少手术人员及患者 X 线暴露时间[15-17]。

在以 DCB 行血管成形术之前先行 DA 治疗可使药物(如紫杉醇)更好地渗透入动脉壁,促进药物摄取和利用,最大限度地避免切除顽固斑块所致局部炎症,降低新生内膜过度增生风险[18-19]。目前在外周血管床上使用 DCB 存在两个主要问题:一是血流限制性夹层风险高,增加以球囊扩张支架进行补救治疗的概率;二是 DCB 治疗严重钙化血管病变预后较差[13]。研究[20-21]报道,单纯 PTA 治疗支架使用率为 12.6%。另一项亚组分析[22]结果显示,对于 DCB 血管成形术后的夹层,即使不植入支架,也不会导致不良结果。TEPE 等[13]发现,对于钙化病变,在抗增殖治疗前使用减容装置进行血管准备,可能对 DCB 治疗更有益。

3 DCB、DA 治疗 CFPAL

目前 DCB 主要用于治疗简单血管病变和 TASC Ⅱ A、B 型病变。MICARI 等[23]认为 DCB 对于长段股浅动脉(superficial femoral artery, SFA)病变治疗效果较好,该研究采用 DCB 治疗 105 例存在 SFA 病变的 CFPAL 患者,病变血管平均长度为(251±71)mm,其中钙化病变占 63.4%,完全闭塞占 49.5%,病变的复杂性导致植入支架率相对较低(10.9%),随访 12 个月时血管通畅率为 83.2%、TLR 率仅 4%,提示该法具有持续显著的临床效益,且踝肱指数(ankle-brachial index, ABI)、卢瑟福分级和生活质量评价结果均良好;但该研究属于非随机无对照临床试验,缺乏可比较性,需进一步完善。SHAMMAS 等[24]开展另一项单中心临床研究,对符合要求的 75 例新发或再发性股腘动脉病变患者进行回顾性分析,其中 50 例接受 DA+普通 PTA 治疗、25 例接受 DA+DCB 治疗,术后 12 个月 2 组免干预 TLR 率分别为 68.0%、94.7%($P=0.002$),16 个月分别为 54.0%、94.4%($P=0.002$),表明 DA+DCB 的临床效果明显优于 DA+普通 PTA。CIOPPA 等[25]对 30 例有限制性跛行($n=18$)及严重肢体缺血($n=12$)患者(卢瑟福分级 4.2±1.2)先给予 DA 治疗,随后进行 DCB 扩张,根据术中情况决定是否植入支架,手术成功率为 100%,仅 2 例行补救性支架植入;术后随访 1 年,保肢率为 100%,3 例合并 1 型糖尿病患者出现再狭窄,需再次手术干预,术后一期通畅率>90%。

SCHMIDT 等[26]观察 260 例 CFPAL 患者共 288 处肢体病变,病变血管平均长度为(24.0±10.2)mm,平均 ABI 为 0.56±0.22,严重肢体缺血发生率达 26.4%,经 DCB 治疗后 1 年病变血管通畅率为 79.2%,明显高于既往研究[27]报道的 22%～34%;但 DCB 治疗后随访 2 年,血管通畅率下降至 53.7%,可能与手术操作的复杂性和患者本身合并多种基础疾病

有关。值得一提的是,该组对于 288 处病变中的 83 处在 DCB 血管成形术前进行血管腔内减容治疗(包括 DA、机械切除、激光消融),接受减容治疗的病变血管术后 1 年及 2 年平均通畅率分别为(85.3±4.3)%和(64.0±6.1)%,相较于未接受减容治疗者[(76.8±3.2)%和(49.6±4.0)%)]有明显优势。

4 DCB、DA 治疗 ISR

传统 ISR 血管成形术后 6 个月血管开放率仅为 27%,收益期过短,效果欠佳[28]。STABILE 等[29]采用 DCB 治疗 39 处 SFA 病变后 ISR,术后随访 12 个月,一期通畅率为 92%。目前对于 DCB 治疗股腘动脉 ISR 的有效性和安全性仍存在争议。有研究[30]对合并糖尿病 ISR 患者(多数患者出现危重肢体缺血,超过 1/2 患者存在 Tosaka Ⅲ级 ISR)分别给予紫杉醇 DCB 或单纯 PTA 治疗,术后 12 个月 DCB 组与单纯 PTA 组一期通畅率分别为 80.5%及 28.2%,但第 3 年 2 组 TLR 发生率分别为 40%和 43%,提示 DCB 治疗 ISR 并无远期优势。现有研究[31]表明,单纯采用包括 DA 在内的血管腔内减容治疗 ISR 并不能获得较好的通畅率。对于 DCB 单独或联合 DA 治疗外周动脉 ISR 疗效尚待观察。

综上所述,DCB 单独或联合 DA 治疗 CFPAL 的安全性及有效性均较好,但其对于更复杂的腔内病变(如 ISR)的可行性及疗效仍需进一步探索。

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