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·临床研究 Clinical research·

# 紫杉醇药物涂层球囊扩张冠状动脉支架内再狭窄病变增加远期管腔面积

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**【摘要】 目的** 探讨以单纯紫杉醇药物涂层球囊(DCB)扩张冠状动脉介入治疗术后支架内再狭窄(ISR)病变段,观察远期靶血管管腔面积,从而证实 DCB 在 ISR 病变中的作用。**方法** 选取 4 例符合DCB 适应证 ISR 患者,按照标准流程在充分预扩张基础上予以紫杉醇 DCB 扩张病变段,不植入支架。术后即刻及术后 9 个月采用冠状动脉造影和血管内超声检测患者最小管腔横截面积(MLA)、支架横截面积(SA)和血管内膜增生状况。**结果** 4 例患者单纯紫杉醇 DCB 治疗后即刻造影显示靶血管扩张段无夹层,无明显残余狭窄。术后 9 个月造影显示所有患者靶血管扩张段管腔通畅,病变段未见明显再狭窄,TIMI 血流 3 级;血管内超声检测显示 MLA 均较术后即刻显著增加,SA 呈增加趋势,内膜增生呈抑制趋势。**结论** 单纯 DCB 扩张 ISR 病变可增加远期管腔面积,避免二次支架植入,降低再次 ISR 风险,并通过局部释放紫杉醇作用于管壁,抑制内膜过度增生。

**【关键词】** 药物涂层球囊; 支架内再狭窄; 远期管腔面积扩张
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**Long-term lumen area enlarged in coronary in-stent restenosis after the treatment of paclitaxel drug-coated balloon dilatation** *LIU Rong, MA Shixing, ZHAO Gang, HANG Jingyu, WEI Meng, LU Zhigang. Department of Cardiology, Affiliated Sixth People's Hospital of Shanghai Jiaotong University, Shanghai 200233, China*

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**【Abstract】 Objective** To investigate the effect of paclitaxel drug-coated balloon (DCB) dilatation in treating coronary in-stent restenosis (ISR) occurring after drug-eluting stent (DES) implantation, and to observe the long-term changes of the target vascular lumen area in order to clarify the curative effect of paclitaxel DCB in treating ISR. **Methods** Four patients with ISR whose clinical condition met the DCB indication were

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selected. According to the standard process, sufficient pre-expansion of ISR was performed first, then paclitaxel DCB dilatation was carried out to dilate the lesion segment of ISR, and no stent was implanted. Both coronary angiography and intravascular ultrasound (IVUS) were performed immediately after the treatment as well as 9 months to measure the minimum lumen area (MLA) and cross-sectional area (SA) of the stent, and the intimal hyperplasia was also been evaluated. **Results** In all 4 patients, angiography performed immediately after paclitaxel DCB dilatation showed that neither dissection of the dilated segment of the target artery nor obvious residual stenosis was observed. Angiography performed 9 months after the treatment revealed that all dilated segments of the target arteries were patent, and no pronounced restenosis of stent segment was seen. IVUS examination was indicated that MLA became enlarged, SA showed an increasing trend, and intimal hyperplasia showed a tendency to be inhibited. **Conclusion** For the treatment of ISR, pure paclitaxel DCB dilatation can obtain long-term lumen area enlargement, thus, repeated stent implantation can be avoided, which, in turn, can reduce the risk of ISR recurrence. Paclitaxel DCB dilatation can locally release paclitaxel, which has curative effect on the coronary artery wall to inhibit the excessive proliferation of intima. (J Intervent Radiol, 2017, 26: 367-369)

【**Key words**】 drug-coated balloon; in-stent restenosis; long-term lumen area enlargement

单纯球囊扩张冠状动脉目前仅用于少部分双联抗血小板有禁忌或不适用支架植入患者,并受限于扩张后再狭窄、负性重构及内膜增生。药物洗脱支架(DES)应用使得经皮冠状动脉介入治疗(PCI)术后支架内再狭窄(ISR)和靶血管再次血运重建明显减少,但由于越来越多高危及复杂冠状动脉病变患者接受介入治疗,ISR 发生率仍高达 5%～20%[1]。研究显示药物涂层球囊(DCB)可减少内膜增生[2-4],增加血管原位病变远期管腔面积[5],用于治疗裸支架植入术后 ISR 远期效果良好[6-9]。DCB 已独立应用于 ISR 病变,用于药物涂层支架(DCS)植入术后ISR 尚未见相关报道。本研究旨在观察单纯 DCB 扩张后是否能改善 ISR 远期管腔面积变化。

## 1　材料与方法

本研究前瞻性观察单纯紫杉醇 DCB 治疗 DCS 植入术后 ISR 病变的效果。入选 4 例 DCS 植入术后 ISR 患者均为男性,平均年龄为 60.75 岁,平均随访时间 284 d, 术后常规接受口服氯吡格雷和阿司匹林双抗治疗。4 例患者病变血管均为左前降支,冠状动脉造影评估靶血管至少采用 2 个及以上不同体位,血管无重叠,证实为 DCS 内 ISR。ISR 定义为治疗段血管造影直径狭窄≥50%。

采用非顺应性球囊充分预扩张,扩张压力＞命名压, 球囊-血管直径比率 0.8～1.0 或比血管小 0.5 mm[10-11];冠状动脉造影提示无夹层或 A、B 类夹层、TIMI 血流 3 级和残余狭窄≤30%后, 将与预扩张同直径 SeQuent Please DCB(德国 B.Braun 公司)覆盖预扩张部位并超出边缘各 2～3 mm(DCB 在操作过程中主要作为药物递送及后扩装置,不能用手触摸, 不能用 0.9%氯化钠溶液或其它液体浸泡,要尽可能快地送达病变部位), 扩张时使用适中压力(通常为 7 atm),至少扩张 30 s 以上并即刻造影,同时采用血管内超声检测最小管腔横截面积(MLA)、支架横截面积(SA)和血管内膜增生。术后 9 个月复查冠状动脉造影及血管内超声。

## 2　结果

4 例患者单纯紫杉醇 DCB 治疗后即刻造影显示,靶血管扩张段无夹层,无明显残余狭窄,TIMI 血流 3 级。术后 9 个月复查造影显示所有患者靶血管扩张段管腔通畅, 支架段未见明显再狭窄,TIMI 血流 3 级; 血管内超声检测显示 MLA 均较术后即刻显著增加(平均增加 1.35 $mm^2$),SA 呈增加趋势(平均增加 0.11 $mm^2$),内膜增生呈抑制趋势(平均下降 13.23%),见表 1。

**表 1**　单纯紫杉醇 DCB 治疗后血管内超声检测对比

| 患者 | 术后即刻 | | | 术后 9 个月 | | |
|---|---|---|---|---|---|---|
| | MLA/$mm^2$ | SA/$mm^2$ | 内膜增生/% | MLA/$mm^2$ | SA/$mm^2$ | 内膜增生/% |
| 1 | 4.04 | 7.17 | 43.7 | 5.27 | 7.54 | 30.1 |
| 2 | 3.19 | 8.56 | 62.7 | 4.70 | 8.76 | 46.3 |
| 3 | 4.69 | 11.95 | 60.8 | 6.44 | 11.44 | 43.7 |
| 4 | 6.08 | 11.45 | 46.9 | 6.97 | 11.83 | 41.1 |

注: MLA:最小管腔横截面积;SA:支架横截面积

## 3　讨论

单纯球囊扩张最主要局限性在于急性管腔回缩,可导致管腔横截面积丢失达 48%以上[12],再狭窄通常发生于球囊扩张后 2～3 个月。单纯球囊扩张患者初始 PCI 术后 180 d 内有 50%发生再狭窄,

25%患者有＞30%管腔丢失[13]。支架使用及发展正是基于这个原因。

DCB 技术可减少原位病变、外周血管 ISR 比率。目前该技术在我国逐渐得到推广[14]。本研究显示紫杉醇 DCB 扩张治疗 DCS 植入术后 ISR 患者术后 9 个月随访时 MLA、SA 较术后即刻有增加趋势，内膜增生呈抑制趋势，考虑可能与紫杉醇改善血管重构有关。紫杉醇可通过调节微导管形成及上调凋亡细胞因子抑制平滑肌细胞增殖，DCB 扩张组较 DCS 植入组血管壁凋亡细胞因子浓度更高，不仅可抑制细胞增殖，而且抑制有丝分裂[15]。在 ISR 形成 4 个阶段中，紫杉醇作用于后 2 个阶段（平滑肌细胞增殖和基质细胞形成），分别从第 1 天和第 7 天启动。紫杉醇作为非细胞周期阻断剂，抑制细胞增殖；在 ISR 早期抑制平滑肌细胞核基质增殖，意味着抑制其级联反应启动。

作为前瞻性研究 DCB 在 ISR 病变中作用的一部分，本研究有诸多局限性，如样本量少、无法作队列研究等。但从研究结果可得出，单纯 DCB 扩张有助于增加 ISR 患者远期 MLA，为进一步研究打下了坚实基础。

总之，本研究显示单纯 DCB 扩张 ISR 病变可增加远期管腔面积，避免二次支架植入，降低再次 ISR 风险，并通过局部释放药物作用于管壁，抑制内膜过度增生。

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