

· 临床研究 ·

老年药物洗脱支架再狭窄及影响因素分析

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【摘要】 目的 调查冠心病经皮冠状动脉介入治疗 (PCI) 患者药物洗脱支架再狭窄 (DES-ISR) 现状及相关因素。**方法** 将 2018 年 6 月至 2021 年 6 月陆军军医大学第二附属医院收治的 536 例行 PCI 手术治疗的冠心病患者纳为研究对象, 根据患者行 PCI 手术时的年龄, 将其分为老年组 ($n=330$) 及青中年组 ($n=206$)。术后随访 6~12 个月, 统计不同年龄段 PCI 手术患者 DES-ISR 发生率, 根据造影结果将患者分为 ISR 组及非 ISR 组, 分别分析影响不同年龄段冠心病 PCI 手术患者 DES-ISR 的相关因素。采用 SPSS 20.0 软件进行数据分析。根据数据类型, 组间比较分别采用 t 检验及 χ^2 检验。**结果** 老年及中青年 PCI 患者术后 DES-ISR 发生率分别为 18.18% (60/330) 与 15.53% (32/206), 差异无统计学意义。老年 PCI 术后 ISR 组中合并糖尿病、合并分叉、钙化病变及弥漫狭窄病变、术后服药依从性差、支架断裂、支架扩张不足、术前 Gensini 评分、支架直径、支架长度、支架个数以及空腹血糖水平高于非 ISR 组, 差异均有统计学意义 (均 $P<0.05$)。中青年 PCI 术后 ISR 组中合并高血压、吸烟、饮酒者占比高于非 ISR 组, Gensini 评分及低密度脂蛋白胆固醇水平平均高于非 ISR 组, 差异均有统计学意义 (均 $P<0.05$)。**结论** 影响不同年龄段 CHD 患者 PCI 术后 DES-ISR 发生率的相关因素不尽相同, 老年 PCI 术后 DES-ISR 发生风险主要与其冠状动脉病变严重程度及支架植入状况相关, 而中青年 PCI 术后 DES-ISR 发生风险则主要与其术后不良生活习惯相关。

【关键词】 冠心病; 经皮冠状动脉介入治疗; 药物洗脱支架再狭窄; 影响因素

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Restenosis of drug-eluting stents in elderly patients and its influencing factors

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【Abstract】 Objective To investigate the current status and related factors of in-stent restenosis (ISR) in patients with coronary heart disease (CHD) undergoing percutaneous coronary intervention (PCI) with drug-eluting stents (DES). **Methods** A total of 536 CHD patients undergoing PCI in our hospital from June 2018 to June 2021 were enrolled as the study subjects. According to their age, they were divided into elderly group ($n=330$) and young and middle-aged group ($n=206$). At 6-12 months of follow-up, the incidence rate of DES-ISR was observed in the patients of different age groups. According to the imaging results, the patients were divided into ISR group and non-ISR group, and the related factors affecting DES-ISR were analyzed. SPSS statistics 20.0 was used for statistical analysis. Data comparison between two groups was performed using student's t test or χ^2 -square test depending on data type. **Results** The incidence rate of DES-ISR after PCI was 18.18% (60/330) in the elderly group and 15.53% (32/330) in the young and middle-aged group, and there was no statistical significance between the two groups. The elderly ISR group had obviously larger proportions of diabetes mellitus, bifurcation, calcification, diffuse stenosis, poor postoperative medication compliance, and under-expansion of the stent and stent fractures, higher preoperative Gensini score, larger stent diameter and longer stent length and higher stent number, and higher count fasting blood glucose level when compared with those without ISR group (all $P<0.05$). In the young and middle-aged patients with ISR, larger proportions of hypertension, smoking and drinking, and higher Gensini score and low-density lipoprotein level were observed than in those without ISR (all $P<0.05$). **Conclusion** The related factors affecting the incidence of DES-ISR after PCI in CHD patients of different age groups are not the same. The risk of DES-ISR after PCI is mainly related to the severity of coronary artery lesion and stent implantation status in the elderly, while postoperative bad living habits in the young and middle-aged patients.

【Key words】 coronary heart disease; percutaneous coronary intervention; drug-eluting stent restenosis; influencing factors

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经皮冠状动脉介入治疗(percutaneous coronary intervention, PCI)是冠心病(coronary atherosclerotic heart disease, CHD)的主要治疗方法^[1,2]。但术后药物洗脱支架再狭窄(drug eluting stent-in-stent stenosis, DES-ISR)一直是影响手术效果及患者预后的主要问题^[3,4]。当前,关于PCI术后ISR的相关研究较多,但尚无报道对老年及中青年CHD患者PCI术后ISR差异进行分析。本研究旨在探究老年及中青年患者术后ISR差异,为临床制定个性化护理或治疗方案提供参考

1 对象与方法

1.1 研究对象

将2018年6月至2021年6月陆军军医大学第二附属医院收治的行PCI手术治疗,回院复诊时因自身诉求、出现胸闷胸痛症状或心电图改变等原因,进行冠状动脉造影的CHD 536例患者纳为研究对象。(1)纳入标准:均经临床检查确诊为CHD;行PCI手术,置入至少1枚DES。(2)排除标准:合并其他心脏病变;合并自身免疫性疾病;肝肾功能严重障碍;合并恶性肿瘤。

1.2 方法

1.2.1 治疗及随访 所有患者均成功接受PCI治疗,植入支架均为雷帕霉素DES,术后按规定服用相关药物。随访6~12(8.63±1.83)个月,所有患者均因自身诉求或出现胸闷胸痛症状、心电图改变等情况,进行冠状动脉造影检查,根据检查判断其是否发生DES-ISR^[5],并根据造影结果将患者分为ISR组及非ISR组。

1.2.2 资料收集 根据患者行PCI手术时的年龄,将536例患者分为老年组(年龄≥60岁, $n=330$)与中青年组(<60岁, $n=206$)。收集2组患者资料,包括年龄、性别、基础性疾病、术后不良生活习惯、病变部位、是否分叉、病变血管支数、钙化病变、弥漫性狭窄病变、PCI植入支架状况、是否出现支架断裂及支架扩张不足、术后复诊时生化指标、术后服药依从性、患者风险因素及病变因素等。

1.3 统计学处理

采用SPSS 20.0统计软件进行数据分析。计量资料用均数±标准差($\bar{x} \pm s$)表示,采用 t 检验;计数资料用例数(百分率)表示,采用 χ^2 检验。 $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 老年及中青年PCI患者术后DES-ISR发生率比较

老年PCI患者术后DES-ISR发生率为18.18%(60/330),中青年PCI患者术后DES-ISR发生率为15.53%(32/206),差异无统计学意义。

2.2 老年PCI患者术后DES-ISR发生风险的影响因素分析

老年PCI术后ISR组中合并糖尿病、合并分叉、钙化病变、弥漫狭窄病变、术前Gensini评分、支架直径、支架长度、支架个数、空腹血糖水平、术后服药依从性差、支架断裂、支架扩张不足发生率均高于非ISR组,差异均有统计学意义(均 $P < 0.05$;表1)。

2.3 中青年PCI患者DES-ISR发生风险的影响因素分析

中青年PCI术后ISR组患者中合并高血压、吸烟、饮酒情况、Gensini评分及低密度脂蛋白胆固醇水平均高于非ISR组,差异均有统计学意义(均 $P < 0.05$;表2)。

3 讨论

临床数据表示,有超过90%的CHD患者最终选择PCI治疗,但PCI术后再狭窄问题也在一定程度上限制了PCI的全面推广^[6]。有研究表明,PCI术后DES-ISR主要原因是术中操作导致血管内皮细胞完整性被破坏,血管内膜过度增生、重塑^[7]。但除此之外,术后服药依从性、植入支架状况、患者基础性疾病等也是影响DES-ISR的相关因素^[8,9]。

很多研究表明,不同年龄段患者CHD主要危险因素存在差异^[10]。而不同年龄段CHD患者PCI术后DES-ISR相关危险因素是否也存在差异?本研究通过对比发现,中青年及老年CHD患者术后DES-ISR发生率相似,但影响不同年龄段CHD患者PCI术后DES-ISR的相关因素却不尽相同。

整体对比发现,老年及中青年CHD患者的临床特征存在一定的差异,具体表现为老年CHD患者病变血管支数更多,钙化病变及弥漫性狭窄病变更严重,术前Gensini得分更高,提示老年CHD患者病情整体更严峻。而病变部位钙化严重、斑块负荷重、复杂病变等是引起支架断裂及扩张不充分的重要原因。本研究复查IVUS发现,老年CHD患者支架断裂及扩张不足发生率较青中年组更高,提示老年组中因病变严重程度导致的支架断裂及扩张不足占比更高。

表1 老年PCI患者术后DES-ISR发生风险的影响因素分析

Table 1 Analysis of influencing factors of risk of DES-ISR after PCI in elderly patients

Indicators	ISR group(<i>n</i> = 60)	NISR group(<i>n</i> = 270)	<i>t</i> / χ^2	<i>P</i> value
Gender[<i>n</i> (%)]			1.479	0.224
Male	42(70.00)	209(77.41)		
Female	18(30.00)	61(22.59)		
Age[<i>n</i> (%)]			0.055	0.815
60–75 years	33(55.00)	144(53.33)		
>75 years	27(45.00)	126(46.67)		
Underlying diseases[<i>n</i> (%)]				
Diabetes mellitus	13(21.67)	22(8.15)	9.462	0.002
Hypertension	25(41.67)	114(42.22)	0.006	0.937
Hyperlipidemia	8(13.33)	30(11.11)	0.238	0.626
Smoking[<i>n</i> (%)]			0.009	0.925
Yes	13(21.67)	60(22.22)		
No	47(78.33)	210(77.78)		
Drinking[<i>n</i> (%)]			0.572	0.450
Yes	10(16.67)	35(12.96)		
No	50(83.33)	235(87.04)		
Lesion sites[<i>n</i> (%)]			0.135	0.713
Anterior descending branch	36(60.00)	155(57.41)		
Posterior circumflex branch	8(13.33)	31(11.48)		
Right coronary	18(30.00)	89(32.96)		
Left main coronary artery	1(1.67)	3(1.11)		
Presence or absence of bifurcation[<i>n</i> (%)]			6.813	0.009
Yes	8(13.33)	12(4.44)		
No	52(86.67)	258(95.56)		
Number of diseased vessels[<i>n</i> (%)]			0.546	0.761
Single-vessel	33(55.00)	152(56.30)		
Double-vessel	14(23.33)	70(25.93)		
Three-vessel	13(21.67)	48(17.78)		
Calcification[<i>n</i> (%)]	25(41.67)	59(21.85)	10.607	0.001
Diffuse stenosis[<i>n</i> (%)]	26(43.33)	48(17.78)	18.430	<0.001
Gensini score(points, $\bar{x}\pm s$)	66.36±10.25	40.36±6.75	24.286	<0.001
Stent diameter(mm, $\bar{x}\pm s$)	3.07±0.45	3.41±0.61	4.076	<0.001
Stent length(mm, $\bar{x}\pm s$)	30.22±4.05	25.69±3.48	8.843	<0.001
Stent count(pcs, $\bar{x}\pm s$)	1.61±0.25	1.52±0.21	2.896	0.004
Fasting blood glucose(mmol/L, $\bar{x}\pm s$)	6.66±1.23	5.65±1.15	6.075	<0.001
LDL-C(mmol/L, $\bar{x}\pm s$)	2.43±0.24	2.36±0.31	1.642	0.102
PCI time(min, $\bar{x}\pm s$)	63.69±10.67	61.88±12.52	1.039	0.300
Medication compliance[<i>n</i> (%)]			8.827	0.003
Good	52(86.67)	260(96.30)		
Poor	8(13.33)	10(3.70)		
Renal insufficiency[<i>n</i> (%)]			2.591	0.108
Yes	8(13.33)	19(7.04)		
No	52(86.67)	251(92.96)		
Acute coronary syndromes[<i>n</i> (%)]			0.389	0.533
Yes	3(5.00)	9(3.33)		
No	57(95.00)	261(96.67)		
Previous coronary artery bypass grafting[<i>n</i> (%)]			2.166	0.141
Yes	13(21.67)	38(14.07)		
No	47(78.33)	232(85.93)		
Pathological factor[<i>n</i> (%)]			0.014	0.905
Chronic closures	7(11.67)	33(12.22)		
Ostial lesions	53(93.33)	237(87.78)		
Sub-optimal apposition[<i>n</i> (%)]	13(21.67)	36(13.33)	2.696	0.100
Under-expansion of stent[<i>n</i> (%)]	6(10.00)	0(0.00)	22.183	<0.001
Stent fractures[<i>n</i> (%)]	13(21.67)	6(2.22)	34.206	<0.001

PCI; percutaneous coronary intervention; DES-ISR; drug eluting stent-in-stent stenosis; ISR; in-stent restenosis; NISR; no in-stent stenosis; LDL-C; low-density lipoprotein cholesterol.

表 2 中青年 PCI 患者术后 DES-ISR 发生风险的影响因素分析

Table 2 Analysis of influencing factors of risk of DES-ISR after PCI in young and middle-aged patients

Indicators	ISR(<i>n</i> =32)	NISR(<i>n</i> =174)	<i>t</i> / χ^2	<i>P</i> value
Gender[<i>n</i> (%)]			0.167	0.683
Male	23(71.88)	131(75.29)		
Female	9(28.13)	43(24.71)		
Age[<i>n</i> (%)]			0.032	0.858
<45 years	16(50.00)	84(48.28)		
45–59 years	16(50.00)	90(51.72)		
Underlying diseases[<i>n</i> (%)]				
Diabetes mellitus	4(12.50)	20(11.49)	0.027	0.871
Hypertension	16(50.00)	53(30.46)	4.633	0.031
Hyperlipidemia	3(9.38)	13(7.47)	0.137	0.712
Smoking[<i>n</i> (%)]			6.180	0.013
Yes	9(28.13)	20(11.49)		
No	23(71.88)	154(88.51)		
Drinking[<i>n</i> (%)]			6.813	0.009
Yes	9(28.13)	19(10.92)		
No	23(71.88)	155(89.08)		
Lesion sites[<i>n</i> (%)]				
Anterior descending branch	17(53.13)	88(50.57)	0.070	0.791
Posterior circumflex branch	7(21.88)	33(18.97)	0.146	0.702
Right coronary	11(34.38)	56(32.18)	0.059	0.808
Left main coronary artery	0(0.00)	0(0.00)	–	–
Presence or absence of bifurcation[<i>n</i> (%)]			0.279	0.598
Yes	1(3.13)	3(1.72)		
No	31(96.88)	171(98.28)		
Number of diseased vessels[<i>n</i> (%)]			0.253	0.881
Single-vessel	20(62.50)	101(58.05)		
Double-vessel	11(34.38)	68(39.08)		
Three-vessel	1(3.13)	5(2.87)		
Calcification[<i>n</i> (%)]	3(9.38)	15(8.62)	0.019	0.890
Diffuse stenosis[<i>n</i> (%)]	2(6.25)	13(7.47)	0.060	0.807
Gensini score(points, $\bar{x}\pm s$)	48.25±10.54	39.58±7.63	5.538	<0.001
Stent diameter(mm, $\bar{x}\pm s$)	3.02±0.36	3.18±0.45	1.901	0.059
Stent length(mm, $\bar{x}\pm s$)	23.69±4.43	22.78±3.78	1.218	0.225
Stent count(pcs, $\bar{x}\pm s$)	1.32±0.32	1.25±0.25	1.390	0.166
Fasting blood glucose(mmol/L, $\bar{x}\pm s$)	6.22±1.25	5.95±1.16	1.196	0.233
LDL-C(mmol/L, $\bar{x}\pm s$)	2.76±0.32	2.36±0.35	6.017	<0.001
PCI time(min, $\bar{x}\pm s$)	56.69±11.34	57.02±12.05	0.144	0.886
Medication compliance[<i>n</i> (%)]			0.120	0.729
Good	31(96.88)	170(97.70)		
Poor	1(3.13)	4(2.30)		
Renal insufficiency[<i>n</i> (%)]			0.001	0.974
Yes	3(9.38)	16(9.20)		
No	29(90.63)	158(90.80)		
Acute coronary syndromes[<i>n</i> (%)]			0.279	0.598
Yes	1(3.13)	3(1.72)		
No	31(96.88)	171(98.28)		
Previous coronary artery bypass grafting[<i>n</i> (%)]			2.338	0.126
Yes	2(6.25)	3(1.72)		
No	30(93.75)	171(98.28)		
Pathological factor[<i>n</i> (%)]			1.676	0.195
Chronic closures	3(9.38)	7(4.02)		
Ostial lesions	29(90.63)	167(95.98)		
Sub-optimal apposition[<i>n</i> (%)]	7(21.88)	18(10.34)	3.370	0.066
Under-expansion of stent[<i>n</i> (%)]	1(3.13)	0(0.00)	0.910	0.340
Stent fractures[<i>n</i> (%)]	2(6.25)	1(0.57)	2.635	0.105

PCI: percutaneous coronary intervention; DES-ISR: drug eluting stent-in-stent stenosis; ISR: in-stent restenosis; NISR: no in-stent stenosis; LDL-C: low-density lipoprotein cholesterol. –: no datum.

进一步分析发现,影响老年 CHD 患者 PCI 术后 DES-ISR 的因素包括是否分叉、钙化病变、弥漫性病变以及植入支架直径、长度、数量、支架断裂及扩张不足等,说明影响老年 PCI 患者术后 DES-ISR 的主要因素为冠状动脉病变严重程度及支架植入状况。这可能与 CHD 病变越严重,术中操作复杂程度及对血管内皮造成的相关损伤越大,术后 DES-ISR 发生风险越高相关^[11,12]。而影响中青年 CHD 患者 PCI 术后 DES-ISR 的相关因素包括高血压、吸烟、饮酒、术前 Gensini 评分以及低密度脂蛋白胆固醇,这与中青年 CHD 患者社交活动更活跃,更难按照医嘱戒烟戒酒,维持血压平衡,进而增加 PCI 术后 DES-ISR 发生风险相关^[13]。吸烟与动脉斑块及支架狭窄形成的相关机制已逐渐明确^[14]。此外,饮酒会增加心脏及肝脏负担,直接损坏心肌及血管内壁,造成心肌能量代谢障碍,促进动脉粥样硬化及支架狭窄^[15]。

综上,影响不同年龄段 CHD 患者 PCI 术后 DES-ISR 发生率的相关因素不尽相同。但受限于研究设计,本研究并未将所有可能影响 DES-ISR 的相关因素进行分析,且本文为回顾性分析,病例纳入偏倚可能影响结果,可进一步深化研究方案,开展前瞻性分析,增强研究可信度。

【参考文献】

[1] Hoole SP, Bambrough P. Recent advances in percutaneous coronary intervention[J]. Heart, 2020, 106(18): 1380–1386. DOI: 10.1136/heartjnl-2019-315707.

[2] Tsutsui RS, Sammour Y, Kalra A, *et al.* Excimer laser atherectomy in percutaneous coronary intervention: a contemporary review[J]. Cardiovasc Revasc Med, 2021, 25(8): 75–85. DOI: 10.1016/j.carrev.2020.10.016.

[3] Grieshaber P, Oswald I, Albert M, *et al.* Risk of perioperative coronary stent stenosis or occlusion in patients with previous percutaneous coronary intervention undergoing coronary artery bypass grafting surgery[J]. Eur J Cardiothorac Surg, 2020, 57(6): 1122–1129. DOI: 10.1093/ejcts/ezaa003.

[4] Stephan T, Keßler M, Goldberger N, *et al.* Angiographic results after percutaneous coronary interventions in ostial *versus* distal left main lesions[J]. Cardiovasc Revasc Med, 2021, 23(10): 22–27. DOI: 10.1016/j.carrev.2020.08.025.

[5] Ullrich H, Olschewski M, Münzel T, *et al.* Coronary in-stent restenosis: predictors and treatment[J]. Dtsch Arztebl Int, 2021, 118(38): 637–644. DOI: 10.3238/arztebl.m2021.0254.

[6] Lehto HR, Winell K, Pietilä A, *et al.* Outcomes after coronary artery bypass grafting and percutaneous coronary intervention in diabetic and non-diabetic patients[J]. Eur Heart J Qual Care Clin Outcomes, 2022, 8(6): 692–700. DOI: 10.1093/ehjqcco/qcab065.

[7] Ko YG, Kim JS, Kim BK, *et al.* Efficacy of drug-eluting stents for treating in-stent restenosis of drug-eluting stents (from the Korean DES ISR multicenter registry study [KISS])[J]. Am J Cardiol, 2012, 109(5): 607–613. DOI: 10.1016/j.amjcard.2011.10.014.

[8] Zhu Y, Chen M, Liu K, *et al.* Atherogenic index of plasma and the risk of in-stent restenosis in patients with acute coronary syndrome beyond the traditional risk factors[J]. J Atheroscler Thromb, 2022, 29(8): 1226–1235. DOI: 10.5551/jat.63136.

[9] Mittal A, Dhaliwal SS, Bhullar D, *et al.* An in-depth review of retrospective studies to assess the role of vascular brachytherapy for the treatment of complex patients with multiple risk factors for DES-ISR[J]. Rev Cardiovasc Med, 2022, 23(2): 54–60. DOI: 10.31083/j.rcm2302054.

[10] 于哲新, 李虹伟, 顾复生, 等. 北京市大兴区西红门社区居民冠心病危险因素变化分析[J]. 中国全科医学, 2015, 18(28): 3452–3455. DOI: 10.3969/j.issn.1007-9572.2015.28.017.

[11] Shimono H, Kajiya T, Takaoka J, *et al.* Characteristics of recurrent in-stent restenosis after second- and third-generation drug-eluting stent implantation[J]. Coron Artery Dis, 2021, 32(1): 36–41. DOI: 10.1097/MCA.0000000000000945.

[12] Megaly M, Alani F, Cheng CI, *et al.* Risk factors for the development of carotid artery in-stent restenosis: multivariable analysis[J]. Cardiovasc Revasc Med, 2021, 24(5): 65–69. DOI: 10.1097/MCA.0000000000000945.

[13] Peng KG, Yu HL. Characteristic analysis of clinical coronary heart disease and coronary artery disease concerning young and middle-aged male patients[J]. World J Clin Cases, 2021, 9(25): 7358–7364. DOI: 10.12998/wjcc.v9.i25.7358.

[14] Khan SS, Page C, Wojdyla DM, *et al.* Predictive utility of a validated polygenic risk score for long-term risk of coronary heart disease in young and middle-aged adults[J]. Circulation, 2022, 146(8): 587–596. DOI: 10.1161/CIRCULATIONAHA.121.058426.

[15] Mortensen MB, Dzaye O, Bødtker H, *et al.* Interplay of risk factors and coronary artery calcium for CHD risk in young patients[J]. JACC Cardiovasc Imaging, 2021, 14(12): 2387–2396. DOI: 10.1016/j.jcmg.2021.05.003.

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