·临床研究·

合并结缔组织病的冠心病患者冠状动脉病变特点及冠状动脉介入治疗术预后分析

周 力,陈 晖,李卫萍,高红丽,李东宝,赵慧强,姚道阔,李虹伟*
(首都医科大学附属北京友谊医院心血管中心,北京 100050)

【摘 要】 **目的** 探讨合并结缔组织病(CTD)的冠状动脉性心脏病(CAD)患者的冠状动脉病变特点,以及接受经皮冠状动脉介入治疗术(PCI)的长期预后。**方法** 收集106例自2009年1月至2012年12月在北京友谊医院接受PCI治疗CTD患者的临床资料,回顾性分析CTD患者的临床表现和冠状动脉病变特点等,并对CTD患者进行长期随访。**结果** 106例患者中有92例(86.8%)具有≥1个传统冠心病危险因素。78例(73.6%)的患者冠状动脉为多支血管病变,以前降支受累为主(65.1%)。共植入5枚金属裸支架和202枚药物涂层支架。对CTD患者进行了平均时间长达3年的随访,期间共发生主要不良心血管事件(MACE)24例(22.6%),其中心源性死亡13例(12.3%)、支架内血栓形成(ST)10例(9.4%)、靶血管再次血运重建(TVR)15例(14.2%)。**结论** 合并CTD的CAD患者冠状动脉病变以多支病变为主。此类患者接受PCI术后不良事件以ST及TVR多见。

【关键词】 结缔组织病;冠状动脉性心脏病;经皮冠状动脉介入治疗术;预后
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Features of coronary artery lesions and prognosis after percutaneous coronary intervention in patients with coronary artery disease and connective tissue disease

ZHOU Li, CHEN Hui, LI Wei-Ping, GAO Hong-Li, LI Dong-Bao, ZHAO Hui-Qiang, YAO Dao-Kuo, LI Hong-Wei*
(Center for Cardiovascular Diseases, the Affiliated Beijing Friendship Hospital of Capital Medical University, Beijing 100050, China)

【**Abstract**】 **Objective** To investigate the features of coronary artery lesions in the patients suffering from coronary artery disease (CAD) and connective tissue disease (CTD) and their long-term prognosis after percutaneous coronary intervention (PCI). **Methods** A consecutive series of 106 CTD patients who underwent PCI with stent implantation in our hospital between January 2009 and December 2012 were enrolled in this study. After their medical records were collected, the clinical manifestations and coronary artery lesions features were analyzed retrospectively. They were also followed-up for long-term incidences of major adverse cardiac events (MACE). **Results** Ninety-two of the patients (86.8%) had one or more traditional CAD risk factors. Multi-vessel disease was present in the 78(73.6%) patients, with the left anterior descending coronary artery mostly involved (accounting for 65.1%). There were totally 5 bare-metal stents and 202 drug eluting stents implanted. During the follow-up of average 3 years, 24 cases (22.6%) of MACEs were observed, including 13(12.3%) death from cardiac causes, 10(9.4%) of stent thrombosis, and 15 (14.2%) of target vessel revascularization (TVR). **Conclusion** Patients with CTD and CAD are characterized by multi-vessel lesions. Stent thrombosis and TVR are common adverse events in the patients after PCI.

【**Key words**】 connective tissue diseases; coronary artery disease; percutaneous coronary intervention; prognosis
Corresponding author: *LI Hong-Wei*, *E-mail*: *lhw19656@sina.com*

结缔组织病(connective tissue disease, CTD)作为一组自身免疫性疾病,可累及包括心脏在内的全身多个系统;而冠心病(coronary artery disease, CAD)是CTD患者的重要死因;尤其见于系统性红斑狼疮(systemic lupus erythematosus, SLE)、类风湿性关节炎(rheumatoid arthritis, RA)以及大动脉炎的患者[1-3]。研究表明,CTD患者的动脉粥样硬化进程明显加快,其罹患心肌梗死的风险显著高于普通人群[4]。CTD患者发生冠心病的危险因素及临床表现均有其自身特点[5],此类患者的最佳血运重建策略尚有待进一步论证[6]。有研究对CTD患者接受经皮冠状动脉介入治疗术(percutaneous coronary

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通信作者:李虹伟,E-mail:lhw19656@sina.com

intervention, PCI)的预后进行了报道,但结论却不尽相同[7-8]。本研究以合并CTD的CAD患者为研究对象,分析其冠状动脉病变特点及接受PCI治疗的长期预后。

1 对象与方法

1.1 对象

以2009年1月至2012年12月在北京友谊医院心内科住院且接受PCI治疗的连续CTD患者为研究对象,共收集106例,包括RA 54例、SLE 11例、干燥综合征(Sjogren's syndrome, SS)38例,白塞病(Behcet's disease, BD)3例;其中男性17例,女性89例,年龄(60.2±10.1)岁。所有患者均于入选前经风湿科专家已确诊CTD并签署知情同意书;其诊断分别符合美国风湿病学会2009年RA诊断标准、1997年SLE分类标准、欧洲抗风湿病联盟2002年SS诊断标准以及国际白塞病研究组1989年BD诊断标准。

1.2 方法

1.2.1 基本资料收集 对所有研究对象进行完整的病史采集及体格检查,测量身高、体质量和血压,询问吸烟、高血压病、2型糖尿病、血脂代谢异常以及心血管疾病家族史。记录患者CTD病程、激素用量及疗程。入院后均通过彩色多普勒超声心动图测定左室射血分数(left ventricular ejection fraction, LVEF)。入院次日清晨空腹8 h经前臂静脉采血,检测血常规、生化等,以上指标的测定在取血后当日上午由我院检验中心进行操作。

1.2.2 PCI操作及抗血小板治疗 由经验丰富的术者依据当前的指南和共识对患者进行PCI操作,首选经桡动脉入路。所有患者术前均予阿司匹林及氯吡格雷双联抗血小板治疗,术后至少12个月双联抗血小板治疗,继之长期服阿司匹林100 mg或氯吡格雷75 mg, 1次/d。

1.2.3 随访及终点事件判定 在住院期间及出院后追踪随访其主要不良心血管事件(major adverse cardiac events, MACE),包括心源性死亡、心肌梗死(myocardial infarction, MI)、靶血管再次血运重建(target vessel revascularization, TVR)、支架内血栓形成(stent thrombosis, ST)及心力衰竭再住院。

对CTD患者采用门诊或电话的方式进行了长期随访,随访截止日期为2015年12月30日(死亡病例以死亡时间为终止时间),无1例失访患者。

1.3 统计学处理

采用SPSS16.0软件包进行统计学处理。计量资料的统计描述采用均数±标准差表示;计数资料的统计描述采用频数表示。累积事件率采用Kaplan-Meier曲线进行评估。统计学意义的检验均为双侧,以$P<0.05$为差异有统计学意义。

2 结 果

2.1 入选患者的基线特征

入选患者的基线特征见表1。共纳入接受PCI治疗的CTD患者106例,其中非ST段抬高型心肌梗死(non ST-elevation myocardial infarction, NSTEMI)18例,急性前壁MI 20例,急性下壁MI 13例,不稳定型心绞痛(unstable angina pectoris, UAP)55例。院外平均随访时间为36个月(四分位间距32~44个月)。

92例(86.8%)患者具有≥1个传统冠心病危险因素。23例(21.7%)患者有≥1年的激素用药史。45例(42.5%)患者入选时类风湿因子或自身抗体检测结果阳性。

表1 CTD患者的基线特征

Table 1 Baseline characteristics of patients with CTD ($n=106$)

Item	Data
Hypertension[n(%)]	88(83.0)
Diabetes[n(%)]	44(41.5)
Family history of early CAD[n(%)]	12(11.3)
Hyperlipidemia[n(%)]	61(57.5)
Smoking[n(%)]	19(17.9)
BMI>28 kg/m^2[n(%)]	15(14.2)
Previous history of MI[n(%)]	6(5.7)
>1 year steroid treatment[n(%)]	23(21.7)
LVEF<50%[n(%)]	17(16.0)
Serum creatinine level (μmol/L, $\bar{x}\pm s$)	86.2±16.8
White blood cell count>10×10^9/L[n(%)]	20(18.9)
Platelet count<150×10^9/L[n(%)]	6(5.7)
Erythrocyte sedimentation rate(mm/h, $\bar{x}\pm s$)	33.2±18.3
Rheumatoid factor or autoantibody positivity[n(%)]	45(42.5)
C reactive protein level>10 mg/L[n(%)]	39(36.8)
Connective tissue diseases[n(%)]	
Rheumatoid arthritis	54(50.9)
Systemic lupus erythematosus	11(10.4)
Sjogren's syndrome	38(35.9)
Behcet's disease	3(2.8)
Coronary artery diseases[n(%)]	
NSTEMI	18(17.0)
Anterior myocardial infarction	20(18.9)
Inferior myocardial infarction	13(12.2)
Unstable angina pectoris	55(51.9)

CTD: connective tissue disease; CAD: coronary artery disease; BMI: body mass index; MI: myocardial infarction; LVEF: left ventricular ejection fraction; NSTEMI: non ST-elevation myocardial infarction

2.2 冠状动脉造影及介入治疗情况

冠脉造影及介入治疗情况见表2。CTD患者中有73.6%患者冠状动脉表现为多支血管病变,且以前降支受累为主(65.1%);SYNTAX评分为(29.5±5.6)分,Gensini评分为(62.4±7.5)分。共植入207枚支架,其中金属裸支架5枚,药物涂层支架202枚。所有患者中只有32例(30.2%)进行了完全血运重建;有91例(85.8%)植入长支架(>20 mm)。

表2 CTD患者的冠状动脉造影及PCI治疗情况

Table 2 Coronary angiographic characteristics and PCI indices of patients with CTD ($n=106$)

Item	Data
Single vessel disease[n(%)]	16(15.1)
Double vessel disease[n(%)]	12(11.3)
Multivessel disease[n(%)]	78(73.6)
Chronic total occlusion[n(%)]	11(10.4)
SYNTAX score($\bar{x}\pm s$)	29.5±5.6
Gensini score($\bar{x}\pm s$)	62.4±7.5
Stented coronary artery[n(%)]	
Left main	15(14.2)
Left anterior descending	69(65.1)
Left circumflex	32(30.2)
Right	46(43.4)
Average stent length per vessel(mm,$\bar{x}\pm s$)	28.1±13.2
Average number of stents per vessel(n,$\bar{x}\pm s$)	1.7±1.0
Stent length>20 mm[n(%)]	91(85.8)
Bifurcation stent[n(%)]	12(11.3)
Complete revascularization[n(%)]	32(30.2)

CTD: connective tissue disease; PCI: percutaneous coronary intervention

2.3 随访及MACE情况

106例患者住院期间、短期(出院后30 d及院外1年)及长期(平均3年)随访结果见表3。CTD患者于住院期间发生各类MACE共5例(4.7%),长期随访中发生MACE达24例(22.6%)。CTD患者共死亡16例,其中13例(12.3%)死于心源性因素,包括6例MI、4例心力衰竭和3例猝死;还有3例是死于感染或肾功能衰竭。有10例(9.4%)急性MI是由于ST所致,其中2例为亚急性、6例为晚期、2例为极晚期ST。在这10例发生ST的患者中,4例为SLE患者,3例为RA患者,2例为BD患者,1例为SS患者。有15例(14.2%)患者进行了TVR治疗,包括再行PCI 12例,CABG 3例,其中9例患者是在PCI术后1年内进行了TVR。

CTD患者随访3年无MACE生存率为77.5%,见Kaplan-Meier生存曲线(图1)。

3 讨 论

既往研究表明,CTD患者具有较高的MI发病率以及心血管疾病死亡率。目前,降低MI死亡率的最有效方法就是进行PCI或CABG等血运重建治疗,而CTD患者接受PCI治疗后是否确实改善了预后,现在并无确切结论。本研究经过平均3年时间的随访发现,CTD患者接受PCI治疗后其总体死亡率为15.1%,ST的发病率为9.4%,TVR率为14.2%。大型临床研究COMPARE试验[9]对接受依维莫司洗脱支架(EES,雅培公司的XIENCE-V支架)和紫杉醇洗脱支架(PES,波士顿科学公司的TAXUS LIBERTE支架)的冠心病患者进行了回顾性分析及长达2年的随访。我们将本研究的随访结果与COMPARE试验进行了对比,发现CTD患者PCI术后2年的累积MACE发生率较COMPARE试验中的冠心病患者升高,其中尤以MI、ST和TVR的发生率显著升高(表4)。

本研究表明,传统冠心病危险因素中,CTD患者的高血压及高脂血症发病率较高,而吸烟及肥胖的比例却不高。尽管目前普遍认为传统危险因素在CTD患者并发CAD中仍占据主导地位,但炎症反应对CTD患者的不良预后同样发挥作用[10]。本研究中CRP升高及类风湿因子或自身抗体阳性者不在少数。此外,本研究中CTD患者的冠状动脉病变以

表3 CTD患者院内及短期和长期随访结果

Table 3 Conditions of CTD patients during hospitalization, and short and long term (median 3 years) follow-up

[$n=106$,n(%)]

Item	In hospital	≤30 days postdischarge	≤1 year postdischarge	Long term follow-up(median 3 years)
MACE	5(4.7)	7(6.6)	17(16.0)	24(22.6)
Cardiac death	2(1.9)	2(1.9)	7(6.6)	13(12.3)
MI	4(3.8)	6(5.7)	13(12.3)	18(17.0)
TVR	2(1.9)	2(1.9)	9(8.5)	15(14.2)
Repeat PCI	2(1.9)	2(1.9)	8(7.6)	12(11.3)
Repeat CABG	0(0.0)	0(0.0)	1(0.9)	3(2.8)
Stent thrombosis	2(1.9)	2(1.9)	8(7.6)	10(9.4)
Heart failure	2(1.9)	2(1.9)	4(3.8)	9(8.5)

CTD: connective tissue disease; MACE: major adverse cardiac events; MI: myocardial infarction; TVR: target vessel revascularization; PCI: percutaneous coronary intervention; CABG: coronary artery bypass grafting

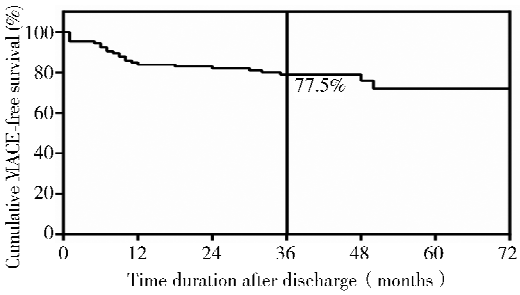


图1 随访3年无MACE生存率

Figure 1 The cumulative MACE-free survival curve of all patients during 3-year follow-up

MACE: major adverse cardiac events

表4 与COMPARE试验2年随访结果比较

Table 4 Two years follow-up results compared with the COMPARE trial

Item	COMPARE trial		This study
	EES group	PES group	CTD group
Age(years)	62.9	63.6	60.2±10.1
Number of patients(*n*)	897	903	106
MACE(%)	9.0	13.7	17.9
Cardiac death(%)	2.2	1.8	7.5
MI(%)	3.9	7.5	14.2
TVR(%)	3.0	7.6	9.4
Stent thrombosis(%)	0.9	3.9	7.6

EES: everolimus eluting stent; PES: paclitaxel eluting stent; CTD: connective tissue disease; MACE: major adverse cardiac events; MI: myocardial infarction; TVR: target vessel revascularization

多支血管病变为主。目前认为[11],CTD患者的冠状动脉病变的病理生理学机制包括动脉粥样硬化、动脉炎、血栓形成、栓塞、痉挛以及血流动力学改变等较多因素。除动脉粥样硬化斑块导致CAD外,CTD患者还常出现冠状动脉瘤样扩张,尤其多见于SLE患者。

本研究观察到,CTD患者的MACE中ST发生率较高,其中超过50%的ST是发生于支架置入后的31 d~1年内,也就是以晚期ST为主。一般来说,除去操作等技术因素,ST多见于复杂病变患者,如急性冠脉综合征、小血管病变、分叉病变、慢性完全闭塞病变以及植入多个或长支架[12]。本研究中有高达85.8%的CTD患者植入长支架;与其他CTD患者相比,白塞病患者的ST发生率最高,达到66.7%;而上述患者均为急性ST段抬高型MI。此外,CTD患者普遍存在内皮功能不全现象,而内皮功能不全与ST的关系早已明确[13]。

本研究受样本量不多的限制,未能就不同的CTD疾病以及CTD疾病活动度对临床预后的影响展开详细描述。作为一个单中心回顾性研究,我们的结论还需大样本、前瞻性的病例对照研究来进一步验证。

综上,合并CTD的CAD患者冠状动脉以多支病变为主;此类患者接受PCI治疗后,长期随访中MI、ST及TVR发生率较高。

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