·临床研究·

经皮冠状动脉介入治疗急性冠脉综合征患者戒烟后残余心血管疾病的风险评估

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【摘 要】 目的 探讨行经皮冠状动脉介入治疗(PCI)的急性冠脉综合征(ACS)患者戒烟后残余心血管疾病的风险。**方法** 本研究基于中国冠心病患者大型登记注册研究(OPT-CAD),纳入2012年1月至2014年2月入选OPT-CAD研究的ACS且行PCI的患者,依据吸烟状态(从未吸烟、正在吸烟及已戒烟1年以上)分为未吸烟、吸烟及戒烟3组,比较3组临床资料及介入手术特征、5年临床随访主要心脑血管不良事件(MACCE)的发生情况。所有的数据分析均基于R语言4.1.2版本,通过Trimatch包进行3组倾向性评分匹配。根据数据类型,组间比较分别采用*t*检验、*Wilcoxon*检验及χ^2检验。采用Kaplan-Meier方法绘制累计事件发生曲线并通过log-rank检验进行组间比较。**结果** 进行倾向性评分匹配后3组患者基线特征基本一致。倾向性评分匹配前,3组1、5年MACCE发生率比较,差异均无统计学意义。倾向性评分匹配后,3组患者1年MACCE发生率差异无统计学意义;吸烟组、戒烟组及未吸烟组患者1年靶血管血运重建率比较,差异有统计学意义[28(3.7%)和24(3.2%)和12(1.6%),$P<0.05$],且吸烟组和戒烟组均显著高于未吸烟组($P<0.05$)。未吸烟组、吸烟组及戒烟组患者5年MACCE发生率、全因死亡率及靶血管血运重建率比较,差异均有统计学意义[94(12.6%)和137(18.3%)和105(14.0%),48(6.4%)和85(11.4%)和59(7.9%),31(4.1%)和58(7.7%)和40(5.3%);均$P<0.01$];吸烟组5年MACCE发生率、全因死亡率和靶血管血运重建率均高于未吸烟组(均$P<0.05$)。不同吸烟状态的3组患者5年内的MACCE发生情况及靶血管血运重建的风险随时间变化呈现不同趋势(log-rank $P<0.01$)。相较于未吸烟组,吸烟组(*HR*=1.51,95%*CI* 1.16~1.96;$P<0.05$)和戒烟组患者(*HR*=1.14,95%*CI* 0.87~1.50;$P>0.05$)5年MACCE发生风险均较高;5年靶血管血运重建的风险,吸烟组(*HR*=1.96,95%*CI* 1.26~3.02;$P<0.05$)和戒烟组(*HR*=1.33,95%*CI* 0.83~2.12;$P>0.05$)均高于未吸烟组。**结论** 吸烟与心血管疾病的复发风险明显相关,戒烟可降低MACCE的发生,但残余风险依然存在。

【关键词】 心血管疾病;吸烟;戒烟;风险

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Residual cardiovascular risk after smoking cessation in patients with acute coronary syndrome undergoing percutaneous coronary intervention

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【Abstract】 Objective To investigate the residual cardiovascular disease risk after smoking cessation in patients with acute coronary syndrome (ACS) undergoing percutaneous coronary intervention (PCI). **Methods** The study was based on a large registry study Optimal Anti-platelet Therapy for Chinese patients with Coronary Artery Disease (OPT-CAD). ACS patients undergoing PCI in the OPT-CAD study from January 2012 to February 2014 were enrolled in the current study and were divided into three groups according to their smoking status (never, current smoking and smoking cessation for more than 1 year): non-smoker, smoker, and former smoker. The three groups were compared in the clinical data and characterizes of the interventional surgery, and the incidence of major adverse cardiovascular and cerebrovascular events (MACCE) in the five-year clinical follow-up visit. All data analysis was based on R language version 4.1.2, and 3 groups of propensity score matching were performed by the Trimatch package. Data comparison between two groups

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was perfomed using *t* test, *Wilcoxon* test or χ^2 test depending on data type. Cumulative event occurrence curves were drawn using the Kaplan-Meier method and compared between two groups by the log-rank test. **Results** The baseline characteristics of the three groups were essentially identical after propensity score matching. There was no significant difference in the incidence of 1- and 5-year MACCE between the three groups before the propensity score matching. After the propensity score matching, there was no significant difference in the incidence of 1-year MACCE among the three groups, but incidence of 1-year target vessel revascularization differed significantly among the smoker group, the former smoker group and the non-smoker group [28(3.7%) *vs* 24(3.2%) *vs* 12(1.6%), $P<0.05$], and the rate in the smoker group and former smoker group were higher than the non-smoker group. There were significant differences among the non-smoker group, the smoker group and the former smoker group in the incidence of 5-year MACCE, all-cause mortality, and target vessel revascularization [94(12.6%) *vs* 137(18.3%) *vs* 105(14.0%), 48(6.4%) *vs* 85(11.4%) *vs* 59(7.9%), 31(4.1%) *vs* 58(7.7%) *vs* 40(5.3%); all $P<0.01$]. The incidence of 5-year MACCE, all-cause mortality and target vessel revascularization in the smoker group were higher than those in the non-smoker group (all $P<0.05$). The incidence of 5-year MACCE and 5-year target vascular revascularization in the three groups with different smoking status tended to differ over time (log-rank $P<0.01$). The risk of 5-year MACCE in the smoker group (*HR*=1.51, 95%*CI* 1.16-1.96; $P<0.05$) and the former smoker group (*HR*=1.14, 95%*CI* 0.87-1.50; $P>0.05$) were higher than that in the non-smoker group. The risk of 5-year target vascular revascularization in the smoker group (*HR*=1.96, 95%*CI* 1.26-3.02; $P<0.05$) and the former smoker group (*HR*=1.33, 95%*CI* 0.83-2.12; $P>0.05$) were higher than that in the non-smoker group. **Conclusion** Smoking is significantly associated with the risk of recurrence in cardiovascular disease. Smoking cessation reduces the incidence of MACCE events, but residual cardiovascular risk remains.

【Key words】 cardiovascular disease; smoking; smoking cessation; risk

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吸烟是影响人类健康,导致心血管疾病流行的重大公共卫生问题。目前,提倡戒烟来降低心血管事件的发生。既往曾有多项研究表明,戒烟可显著降低心血管事件的发生率,并与戒烟的年限明显相关[1-3],也有研究报道戒烟后随着体质量指数增高,患者在心血管病事件方面的获益被消减[4]。2021年发表的PARADOX研究显示,吸烟可诱导抗血小板反应性增强,进而发生心血管缺血事件的发生率降低[5]。CHANCES研究显示,患者戒烟可降低心血管疾病发生风险[6]。本研究针对关于吸烟、戒烟中存在争议较多的问题,通过观察在中国人群的真实世界中,吸烟、戒烟及从未吸烟不同生活方式对急性冠脉综合征(acute coronary syndrome, ACS)行经皮冠状动脉介入治疗(percutaneous coronary intervention, PCI)患者5年心血管预后的影响,为改善患者不良生活方式提供依据。

1 对象与方法

1.1 研究对象

OPT-CAD研究[7]是中国人民解放军北部战区总医院韩雅玲院士牵头的一项中国大规模、前瞻性注册研究(美国国立健康研究院 clinicaltrials.gov 研究注册号:NCT01735305),我国31个省、市、自治区的109家中心参加,2012年1月至2014年2月共计入选14032例正在至少1种抗血小板药物治疗的冠心病患者。本研究基于OPT-CAD研究,纳入标准:(1)患者经门诊或住院确诊为ACS且行PCI;(2)年龄≥18岁;(3)正在服用至少1种抗血小板药物;(4)同意参加并签署知情同意书。排除标准:(1)合并严重身心疾病且预期寿命<6个月的患者;(2)由研究者判定、患者不能够完成随访(如言语或精神障碍等);(3)正在参加另一项临床研究尚未获取主要终点指标;(4)获得血液标本时已发生肝素诱导的血小板减少症。本研究入选的患者中,排除了OPT-CAD研究中稳定型冠心病患者2002例,未行PCI患者2967例,戒烟时间<1年患者716例,最终纳入ACS且行PCI的患者8347例。依据吸烟状态分为3组,分别为未吸烟组(从未吸烟患者,$n=3977$),吸烟组(正在吸烟患者,$n=3541$),戒烟组(戒烟1年以上患者,$n=829$)。本研究方案获得中国人民解放军北部战区总医院伦理委员会批准[伦理号K(2012)17号]。所有患者均签署知情同意书并自愿完成指定的后续评估。

1.2 方法

1.2.1 临床资料收集 各中心设负责人按纳入和排除标准筛查并入选受试者和填写病例报告表,并通过远程的独立账号和密码登录由中国人民解放军北部战区总医院开发的电子数据收集系统。

1.2.2 随访及研究终点 通过电话或门诊于PCI后5年内每年对入选患者进行随访。主要终点为5年随访期间发生的主要不良心脑血管事件(major adverse cardiovascular and cerebrovascular event,

MACCE),即包括心源性死亡、心肌梗死、缺血性脑卒中及靶血管血运重建的复合终点;次要观察终点为 5 年随访期间发生的全因死亡、心源性死亡、心肌梗死、缺血性卒中及靶血管血运重建率。

1.3 统计学处理

所有的数据分析均基于 R 语言 4.1.2 版本,使用其 gtsummary 和 survival 包进行统计描述与数据分析,通过 Trimatch 包进行 3 组倾向性评分匹配。符合正态分布的计量资料用均数±标准差($\bar{x}\pm s$)表示,采用 t 检验;非正态分布的计量资料,用中位数(四分位数间距)[$M(Q_1,Q_3)$]表示,采用 *Wilcoxon* 检验。计数资料用例数(百分率)表示,采用 χ^2 检验。3 组基线资料倾向性评分匹配。采用 Kaplan-Meier 方法绘制累计事件发生曲线并通过 log-rank 检验进行组间比较。$P<0.05$ 为差异有统计学意义。

2 结 果

2.1 3 组患者基线资料比较

本研究共入选行 PCI 的 ACS 患者 8 347 例,其中未吸烟组 3 977 例(47.7%),吸烟组 3 541 例(42.4%),戒烟组 829 例(9.9%)。3 组患者年龄、男性、高血压、糖尿病、卒中、贫血、外周血管疾病、既往 PCI、既往心肌梗死发病比例,患者基线左室射血分数、血清胆固醇、血清甘油三酯、血清低密度脂蛋白、eGFR,及患者口服阿司匹林、倍他乐克、钙离子拮抗剂药物应用比例比较,差异均有统计学意义($P<0.05$;表 1)。倾向性评分匹配后 3 组患者基线特征基本均衡,详见表 2,图 1。

表 1 3 组患者基线资料比较

Table 1 Baseline characteristics of patients among three groups

Item	Overall (n=8 347)	Non-smoker group (n=3 977)	Smoker group (n=3 541)	Former smoker group (n=829)	P value
Gender[n(%)]					<0.01
Female	2 022(24.2)	1 780(44.8)	201(5.7)	41(5.0)	
Male	6 325(75.8)	2 197(55.2)	3 340(94.3)	788(95.0)	
Age(years, $\bar{x}\pm s$)	60.6±10.8	63.2±10.4	57.1±10.3	62.8±9.8	<0.01
BMI(kg/m^2, $\bar{x}\pm s$)	24.6±3.0	24.5±3.0	24.7±2.9	24.6±2.8	0.07
Hypertension[n(%)]	4 948(59.3)	2 570(64.6)	1 826(51.6)	552(66.6)	<0.01
Diabetes mellitus[n(%)]	2 094(25.1)	1 127(28.4)	726(20.5)	241(29.1)	<0.01
Stroke[n(%)]	613(7.3)	279(7.0)	238(6.7)	96(11.6)	<0.01
Anemia[n(%)]	815(9.8)	472(11.9)	247(7.0)	96(11.6)	<0.01
PVD[n(%)]	115(1.4)	57(1.4)	35(1.0)	23(2.8)	<0.01
Prior PCI[n(%)]	1 288(15.4)	605(15.2)	454(12.8)	229(27.6)	<0.01
Prior MI[n(%)]	913(10.9)	374(9.4)	355(10.0)	184(22.2)	<0.01
eGFR[ml/(min · 1.73m^2), $M(Q_1,Q_3)$]	107.6(85.3,132.8)	104.5(82.2,130.4)	112.1(90.7,136.9)	101.8(79.5,125.9)	<0.01
LVEF[%, $M(Q_1,Q_3)$]	61.0(56.0,66.0)	61.0(56.0,66.0)	61.0(55.0,66.0)	61.0(55.0,66.0)	0.03
TG[mmol/L, $M(Q_1,Q_3)$]	1.6(1.1,2.2)	1.5(1.1,2.2)	1.6(1.1,2.3)	1.5(1.1,2.1)	0.01
TC[mmol/L, $M(Q_1,Q_3)$]	4.2(3.5,5.0)	4.2(3.6,5.1)	4.3(3.5,5.0)	3.9(3.3,4.6)	<0.01
LDL-C[mmol/L, $M(Q_1,Q_3)$]	2.42(1.8,3.1)	2.43(1.8,3.2)	2.5(1.8,3.1)	2.2(1.6,2.8)	<0.01
HDL-C[mmol/L, $M(Q_1,Q_3)$]	1.0(0.8,1.2)	1.0(0.9,1.3)	1.0(0.80,1.2)	1.0(0.8,1.1)	<0.01
Aspirin[n(%)]	8 232(98.6)	3 910(98.3)	3 510(99.1)	812(98.0)	<0.01
Clopidogrel[n(%)]	8 206(98.3)	3 907(98.2)	3 485(98.4)	814(98.2)	0.81
Beta blocker[n(%)]	6 462(77.4)	3 142(79.0)	2 667(75.3)	653(78.8)	<0.01
ACEI/ARB[n(%)]	5 957(71.4)	2 845(71.5)	2 504(70.7)	608(73.3)	0.32
Statins[n(%)]	8 079(96.8)	3 848(96.8)	3 420(96.6)	811(97.8)	0.21
CCB[n(%)]	1 478(17.7)	820(20.6)	491(13.9)	167(20.1)	<0.01
PPI[n(%)]	3 144(37.7)	1 473(37.0)	1 347(38.0)	324(39.1)	0.53

BMI: body mass index; PVD: peripheral vascular disease; PCI: percutaneous coronary intervention; MI: myocardial infarction; eGFR: estimated glomerular filtration rate; TG: triglyceride; TC: total cholesterol; LDL-C: low-density lipoprotein cholesterol; HDL-C: high-density lipoprotein cholesterol; LVEF: left ventricular ejection fraction; ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotension receptor blockers; CCB: calcium channel blocker; PPI: proton pump inhibitor.

表2 3组患者基线资料比较(倾向性评分匹配)

Table 2 Baseline characteristics of patients among three groups(propensity score match) (n=749)

Item	Non-smoker group	Smoker group	Former smoker group	P value
Gender[n(%)]				0.90
Female	29(3.87)	28(3.74)	30(4.01)	
Male	720(96.13)	721(96.26)	719(95.99)	
Age(years, $\bar{x}\pm s$)	62.7±9.9	63.0±9.8	62.6±9.8	0.72
Body mass index(kg/m^2, $\bar{x}\pm s$)	24.7±2.7	24.6±2.9	24.6±2.8	0.41
Hypertension[n(%)]	505(67.4)	499(66.6)	500(66.8)	0.90
Diabetes mellitus[n(%)]	222(29.6)	224(29.9)	213(28.4)	0.85
Stroke[n(%)]	73(9.8)	78(10.4)	90(12.0)	0.32
Anemia[n(%)]	77(10.3)	102(13.6)	88(11.8)	0.14
PVD[n(%)]	24(3.2)	14(1.9)	20(2.7)	0.32
Prior PCI[n(%)]	199(26.6)	202(27.0)	197(26.3)	0.90
Prior MI[n(%)]	157(21.0)	163(21.8)	154(20.6)	0.83
eGFR[ml/(min·1.73m^2), $M(Q_1, Q_3)$]	101.3(81.4,122.9)	104.7(83.4,126.4)	101.8(79.4,126.8)	0.31
LVEF[%, $M(Q_1, Q_3)$]	61.0(56.0,66.0)	61.0(55.0,66.0)	61.0(55.0,66.0)	0.35
Triglyceride[mmol/L, $M(Q_1, Q_3)$]	1.4(1.0,2.1)	1.5(1.1,2.1)	1.5(1.1,2.1)	0.22
Total cholesterol[mmol/L, $M(Q_1, Q_3)$]	3.9(3.2,4.6)	4.0(3.3,4.8)	3.9(3.3,4.6)	0.15
LDL-C[mmol/L, $M(Q_1, Q_3)$]	2.1(1.6,2.8)	2.3(1.6,2.9)	2.2(1.6,2.8)	0.14
HDL-C[mmol/L, $M(Q_1, Q_3)$]	0.95(0.77,1.13)	0.95(0.78,1.17)	0.96(0.79,1.13)	0.52
Aspirin[n(%)]	742(99.1)	731(97.6)	736(98.3)	0.09
Clopidogrel[n(%)]	738(98.5)	732(97.7)	735(98.1)	0.52
Beta blocker[n(%)]	587(78.4)	595(79.4)	592(79.0)	0.89
ACEI/ARB[n(%)]	534(71.3)	565(75.4)	549(73.3)	0.21
Statins[n(%)]	738(98.5)	728(97.2)	734(98.0)	0.25
CCB[n(%)]	151(20.2)	129(17.2)	154(20.6)	0.23
PPI[n(%)]	285(38.1)	285(38.1)	298(39.8)	0.72

PVD: peripheral vascular disease; PCI: percutaneous coronary intervention; MI: myocardial infarction; eGFR: estimated glomerular filtration rate; LVEF: left ventricular ejection fraction; LDL-C: low-density lipoprotein cholesterol; HDL-C: high-density lipoprotein cholesterol; ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker; CCB: calcium channel blocker; PPI: proton-pump inhibitor.

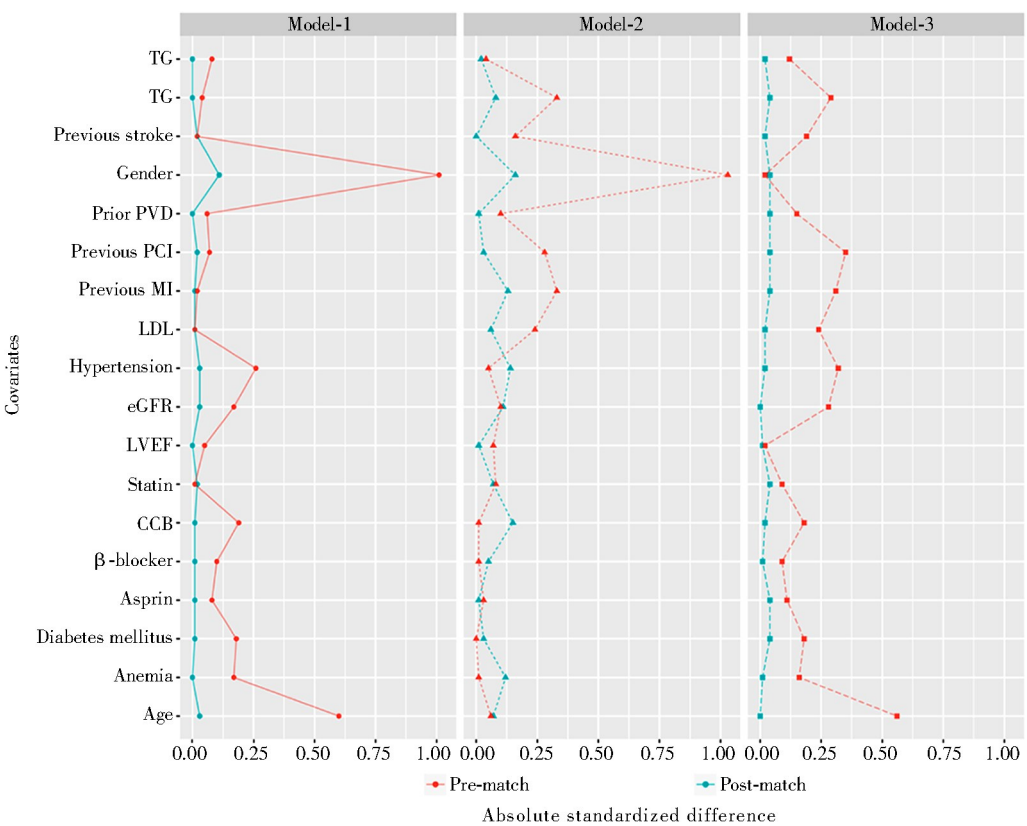

图1 倾向性评分匹配前后各协变量的标准化差异对比

Figure 1 Absolute standardized differences of covariates before and after propensity score matching

TG: triglyceride; TC: total cholesterol; PVD: previous vessel disease; PCI: percutaneous coronary intervention; MI: myocardial infarction; LDL-C: low-density lipoprotein cholesterol; eGFR: estimated glomerular filtration rate; LVEF: left ventricular ejection fraction; CCB: calcium channel blocker.

2.2 3 组患者临床结局指标比较

倾向性评分匹配前,3 组 1、5 年 MACCE 发生率比较,差异均无统计学意义(P>0.05;表 3)。

倾向性评分匹配后,3 组患者 1 年 MACCE 发生率差异无统计学意义;1 年靶血管血运重建在 3 组间差异有统计学意义(P<0.05),且吸烟组和戒烟组均显著高于未吸烟组(P<0.05)。3 组患者 5 年 MACCE 发生率、全因死亡率及靶血管血运重建率比较,差异均有统计学意义(均 P<0.05);吸烟组 5 年 MACCE 发生率、全因死亡率和靶血管血运重建率均高于未吸烟组(均P<0.05);戒烟组 5 年 MACCE 发生率、5 年全因死亡率和靶血管血运重建率均高于未吸烟组,但差异无统计学意义;3 组 5 年心源性死亡、再发心肌梗死及卒中发生率比较,差异均无统计学意义(表 4)。

2.3 生存分析结果

不同吸烟状态的 3 组患者 5 年内的 MACCE 发生情况及靶血管血运重建的风险随时间变化呈现不同趋势(log-rank P<0.01)。相较于未吸烟组,吸烟组(HR = 1.51,95%CI 1.16~1.96;P<0.05)和戒烟组患者(HR = 1.14,95%CI 0.87~1.50;P>0.05)5 年 MACCE 发生风险均较高,吸烟组最高,戒烟组高于未吸烟组;相较于未吸烟组,吸烟组(HR = 1.96,95%CI 1.26~3.02;P<0.05)和戒烟组(HR = 1.33,95%CI 0.83~2.12;P>0.05)5 年靶血管血运重建的风险均较高,吸烟组最高,戒烟组高于未吸烟组(图 2)。

表 3 3 组患者临床结局指标比较

Table 3 Clinical outcomes of patients among three groups [n(%)]

Events	Overall (n=8347)	Non-smoker group (n=3977)	Smoker group (n=3541)	Former smoker group (n=829)	P value
MACCE, 1 year	456(5.5)	222(5.6)	176(5.0)	58(7.0)	0.06
All-cause death	156(1.8)	82(2.1)	49(1.4)	25(3.0)	<0.01
Cardiac death	114(1.4)	64(1.6)	33(0.9)	17(2.1)	<0.01
MI	92(1.1)	39(1.0)	41(1.2)	12(1.5)	0.51
TVR	211(2.5)	89(2.2)	96(2.7)	26(3.1)	0.21
Stroke	107(1.3)	55(1.4)	37(1.0)	15(1.8)	0.22
MACCE, 5 years	1 125(13.5)	536(13.5)	473(13.4)	116(14.0)	0.90
All-cause death	547(6.6)	264(6.6)	217(6.1)	66(8.0)	0.25
Cardiac death	345(4.1)	180(4.5)	127(3.6)	38(4.6)	0.11
MI	231(2.8)	99(2.5)	107(3.0)	25(3.0)	0.32
Stroke	297(3.6)	143(3.6)	120(3.4)	34(4.1)	0.65
TVR	453(5.4)	193(4.9)	215(6.1)	45(5.4)	0.07

MACCE: major adverse cardiovascular and cerebrovascular events; MI: myocardial infarction; TVR: target vessels revascularization.

表 4 3 组患者临床结局指标比较(倾向性评分匹配)

Table 4 Clinical outcomes of patients among three groups(propensity score match) [n=749, n(%)]

Event	Non-smoker group	Smoker group	Former smoker group	P value
MACCE, 1 year	35(4.7)	54(7.2)	55(7.3)	0.06
All-cause death	19(2.5)	21(2.8)	24(3.2)	0.72
Cardiac death	16(2.1)	14(1.9)	17(2.3)	0.90
MI	4(0.5)	10(1.3)	12(1.6)	0.13
TVR	12(1.6)	28(3.7)*	24(3.2)*	0.04
Stroke	6(0.8)	11(1.5)	14(1.9)	0.22
MACCE, 5 years	94(12.6)	137(18.3)*	105(14.0)	<0.01
All-cause death	48(6.4)	85(11.4)*	59(7.9)	<0.01
Cardiac death	34(4.5)	46(6.1)	36(4.8)	0.34
MI	15(2.0)	25(3.3)	24(3.2)	0.22
Stroke	23(3.1)	33(4.4)	31(4.1)	0.41
TVR	31(4.1)	58(7.7)*	40(5.3)	<0.01

Compared with non-smoker group, * P <0.05. MACCE: major adverse cardiovascular and cerebrovascular events; MI: myocardial infarction; TVR: target vessels revascularization.

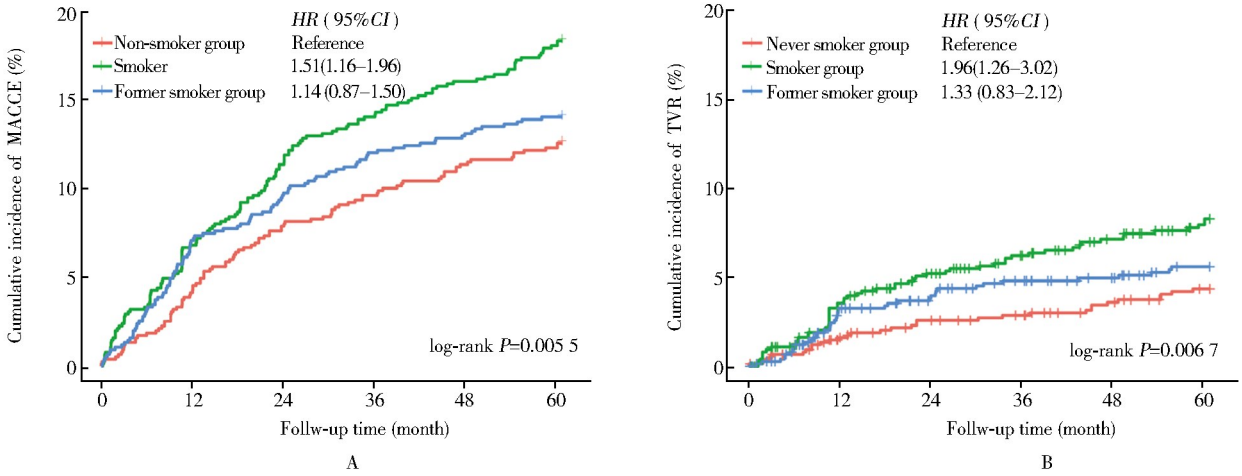

图 2　不同吸烟状态的 3 组患者 5 年随访终点事件的累计发生曲线

Figure 2　Cumulative incidence of endpoints among three groups in 5-year follow-up

A: cumulative incidence of MACCE ; B: Cumulative incidence of TVR.

MACCE: major adverse cardiovascular and cerebrovascular events; TVR: target vessels revascularization.

3　讨　论

本研究基于一项前瞻性、多中心、大样本、真实世界观察性研究,发现吸烟组年龄明显低于其他 2 组,既往心血管疾病及卒中病史低于其他 2 组,以上现象与既往多项研究观察结果一致[8]。本研究入选的均为初次诊断为 ACS 并行 PCI 的患者,从中我们可看出吸烟的危害,即使在既往无冠心病易患因素的年轻男性患者人群中,吸烟仍可导致冠心病的发病明显增加。本研究的关注重点为戒烟后的残余心血管病风险。吸烟的危害众所周知[9],因此社会均倡导戒烟,既往认为戒烟即可降低心血管事件的风险,戒烟后心血管疾病复发的概率便可恢复到从未吸烟人群的水平。戒烟降低心血管事件的风险已被多项研究所论证[10-12]。然而,Chen 等[13]报道的研究对戒烟患者进行长达 8 年的临床随访,发现随着戒烟时间的延长,患者心血管事件可显著降低,但心血管疾病的发生风险仍明显高于从未吸烟的患者。本研究以国人为研究对象,同样发现戒烟后仍然存在残余心血管风险。

潜质未定的克隆性造血(clonal hematopoiesis of indeterminate potential, CHIP)[14]是近年来较为关注的与冠心病发病及预后不良密切相关的危险因素。随着年龄增长,人体细胞会积累体细胞突变[15]。在不同人体组织之间,与年龄相关的突变负荷存在很大异质性,在高度增殖组织中突变率通常更高。人体造血系统中每天约产生 1 010~1 012 个新的血细胞。维持这些细胞产生所需的高增殖率将不可避免地与随机突变的累积有关。在大多数研究中,克隆性造血相关突变与血液肿瘤中发现的突变相似[16]。克隆性造血中最常见的突变基因包括 *DNMT3A*、*TET2*、*ASXL1*、*JAK2*、*TP53* 和 *SF3B1*。近期国外研究曾报导吸烟与 *ASXL1* 基因突变有明显的相关性[17,18],认为吸烟诱导的炎症环境可能促进 *ASXL1* 突变克隆的生长。*ASXL1* 突变与冠心病发病及预后不良密切相关[19,20],*ASXL1* 突变影响炎症细胞(包括 B 细胞、T 细胞、肥大 9 细胞、巨噬细胞等)的功能进而参与动脉粥样硬化发生发展的多个环节,包括内皮损伤、血栓形成、心力衰竭等[21]。

综上,我们推测吸烟可以导致 CHIP 发生风险增高,而戒烟后人群中,部分患者的动脉粥样硬化进程由于 CHIP 的存在而持续进展,导致心血管风险增高。这一假说的证实,将为戒烟后高风险人群的精准识别和治疗提供理论依据。目前尚没有关于戒烟后残余心血管风险与 CHIP 的相关性研究。本中心正在进行的前瞻性探索性研究,将进一步深入研究,揭示戒烟后残余心血管疾病风险的机制,有利于控烟与降低心血管病发生风险。吸烟与心血管疾病的复发风险明显相关,戒烟可降低 MACCE 发生,但残余风险依然存在。

本研究的局限性:(1)本研究只观察患者是否吸烟,对患者每日吸烟量,吸烟的种类未进行统计分析;(2)本研究是真实世界中的回顾性观察研究,有可能存在一定的偏移。

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