· 临床研究 ·

共病负担与老年非 ST 段抬高急性冠脉综合征患者心脑血管不良事件的相关性

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【摘 要】 **目的** 探究年龄校正的查尔森共病指数(aCCI)与老年非 ST 段抬高急性冠脉综合征(NSTE-ACS)患者院外 1 年发生心脑血管不良事件(MACCE)的相关性。**方法** 本研究为回顾性队列研究。收集 2020 年 1 月至 2021 年 11 月首都医科大学附属北京友谊医院心脏中心、老年医学科住院患者 528 例。根据 aCCI 将研究对象分为低 aCCI 组和高 aCCI 组,采用 Kaplan-Meier 法计算不同 aCCI 患者 MACCE 发生率,采用多因素 Cox 回归分析不同 aCCI 组与老年 NSTE-ACS 患者院外 1 年发生 MACCE相关性。采用 SPSS 27.0 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、非参数检验及 χ^2 检验。**结果** 研究对象中位年龄 72(68,76)岁,男性 308 例(58.3%)。高 aCCI 组患者 251 例,低 aCCI 组患者 277 例。高 aCCI 组患者年龄更大,心肌损伤标志物水平更高,容易合并衰弱、多重用药及日常生活能力减低($P<0.05$)。随访 1 年发现,高 aCCI 组患者新发 MACCE 风险明显升高(log-rank $P=0.0002$)。调整多种混杂因素,当 aCCI 为连续变量时,aCCI 每增加 1 个单位时,新发 MACCE 风险将增加 21.3%($HR=1.213$ 95%CI 1.043~1.412;$P=0.012$);当 aCCI 为分类变量,高 aCCI 组新发 MACCE 风险将增加 85.8%($HR=1.858$ 95%CI 1.119~3.083;$P=0.017$)。**结论** 对于老年 NSTE-ACS 患者,较高的 aCCI 与较高的 1 年 MACCE 发生风险相关,早期对老年 NSTE-ACS 进行 aCCI 评估,改善不良预后。

【关键词】 老年人;年龄校正的查尔森共病指数;非 ST 段抬高急性冠脉综合征;风险分层;预后
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Correlation of comorbidity burden with major adverse cardiovascular and cerebrovascular events in older adults with non-ST-segment elevation acute coronary syndrome

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【**Abstract**】 **Objective** To investigate the correlation between age-adjusted Charlson comorbidity index (aCCI) and the occurrence of major adverse cardiovascular and cerebrovascular events (MACCE) within one year after discharge in older adults with non-ST-segment elevation acute coronary syndrome (NSTE-ACS). **Methods** A retrospective cohort study was conducted on 528 inpatients enrolled from Cardiovascular Center and Department of Geriatrics in our hospital between January 2020 and November 2021. The participants were categorized into a low aCCI group and a high aCCI group based on the aCCI value. The incidence of MACCE at different aCCI patients was estimated by Kaplan-Meier method. Multivariate Cox regression analysis was conducted to assess the correlation between different aCCI groups and occurrence of MACCE within one year after discharge in these patients. SPSS statistics 27.0 was used for statistical analysis. Data comparison between two groups was performed using t test, nonparametric test or χ^2 test depending on data type. **Results** The participants had a median age of 72 (68, 76) years, and 58.3% of them (308) were males. The cohort comprised 251 patients in the high aCCI group and 277 patients in the low aCCI group. The high aCCI group exhibited advanced age, higher levels of cardiac injury biomarkers, and larger proportions of frailty, polypharmacy, and lower scores of Activities of Daily Living when compared with the lower aCCI group ($P<0.05$). During one-year of follow-up, the risk of MACCE was significantly higher in the high aCCI group (log-rank $P=0.0002$). After adjusting for various confounding factors, when aCCI was treated as a continuous variable, each one-unit increase in aCCI was associated with 21.3% increase in the risk of MACCE ($HR=1.213$, 95%CI 1.043-1.412; $P=0.012$), and when aCCI was analyzed as a categorical variable, high aCCI group increased 85.8% risk of MACCE ($HR=1.858$, 95%CI 1.119-3.083; $P=0.017$). **Conclusion** In older adults with NSTE-ACS, higher aCCI is associated with increased risk of MACCE. Early assessment of aCCI can improve unfavorable prognosis in these elderly patients.

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【Key words】 aged; age-adjusted Charlson comorbidity index; non-ST-segment elevation acute coronary syndrome; risk stratification; prognosis

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近年来,多项研究致力于探究老年非ST段抬高急性冠脉综合征(non-ST segment elevation acute coronary syndrome,NSTE-ACS)患者,发现此类患者由于功能状态、心理社会关系变化、疾病进展迅速等[1,2],易发生不良预后,亟需临床医师风险分层。对我国60岁及以上老年人调查,慢性疾病患病率可高达81.1%,超过1/3的65岁及以上老年人患有共病[3],共病成为老年人群中的常见现象。目前,国内对于老年NSTE-ACS患者合并共病的研究较少。本研究探究共病负担与老年NSTE-ACS患者预后的关系,旨在为老年NSTE-ACS患者风险分层提供指导作用。

1 对象与方法

1.1 研究对象

收集2020年1月至2021年11月首都医科大学附属北京友谊医院心脏中心、老年医学科住院患者。纳入标准:(1)年龄≥65岁;(2)符合2016年《非ST段抬高急性冠脉综合征诊断及治疗指南》[4]中疾病的诊断标准。排除标准:(1)患者拒绝或无法接受衰弱评估;(2)恶性肿瘤终末期、终末期肾病、严重肝功能不全、急性感染、重度痴呆、完全失能患者。所有患者均签署知情同意书。本研究经首都医科大学附属北京友谊医院医学伦理委员会批准(2020-P2-097)。

1.2 方法

收集患者人口学资料、空腹化验指标及超声心动图指标,特别收集老年综合评估资料和随访资料。

1.2.1 老年综合评估资料 所有老年综合评估均由两名固定的专业护士完成。(1)生活能力:采用巴氏量表,其中0~60分代表日常生活明显需要依赖,61~100分代表日常生活基本不需外力辅助;(2)营养状况:采用微型营养评定简表,其中12~14分为正常营养状况,8~11分为有营养不良的风险,0~7分为营养不良;(3)衰弱情况:采用FRAIL量表,其中3~5分为衰弱,0~2分为非衰弱;(4)多重用药:定义为同时服用5种及以上药物;(5)睡眠障碍:定义为入睡困难,需要长期服用助眠药物。

1.2.2 评估方法 根据年龄校正的查尔森共病指数(age-adjusted Charlson comorbidity index,aCCI)评估患者合并症负担,通过查尔森共病指数(Charlson comorbidity index,CCI)评估19项合并症并计算合并症负担。在此基础上计算aCCI,50~60岁加1分,60~70岁加2分,70~80岁加3分,≥80岁加4分[5]。根据得分分为低aCCI组(aCCI得分<5分)和高aCCI组(aCCI得分≥5分)。

1.2.3 随访资料 出院后在第6,12个月由专业的随访人员进行门诊随访或电话随访。随访的主要终点事件为心脑血管不良事件(major adverse cardiovascular and cerebrovascular events, MACCE),包括再发心绞痛、再发心肌梗死、再发血运重建、卒中、再发心力衰竭和心源性死亡。

1.3 统计学处理

采用SPSS 27.0统计软件进行数据分析。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,采用非参数检验。计数资料用例数(百分率)表示,采用χ^2检验。绘制Kaplan-Meier曲线比较不同aCCI组院外发生MACCE的风险。采用多因素Cox回归分析并绘制森林图表示老年NSTE-ACS患者院外发生MACCE的影响因素,以*HR*和95%*CI*展示。P值取双尾,P<0.05表示差异有统计学意义。

2 结 果

2.1 不同共病患者基线资料情况

研究对象年龄65~90岁,中位年龄72(68,76)岁;男性308例,女性220例;低aCCI组患者占比52.5%(277/528),高aCCI组患者占比47.5%(251/528)。

两组患者相比,高aCCI组年龄更大,非ST段抬高型急性心肌梗死(non-ST-segment elevation myocardial infarction, NSTEMI)患病占比更大,全球急性冠脉事件注册评分(global registry of acute coronary events, GRACE)更高;除此之外,高aCCI组心肌损伤标志物水平更高,血红蛋白水平更低,同时此类患者肌酐清除率更低,尿酸水平更高;在超声心动图方面,高aCCI组左房内径及左室收缩末内径更大,而左室射血分数更低;并且发现高aCCI组容易合并日常生活能力减退、衰弱和多重用药,差异均有统计学意义(P<0.05;表1)。

2.2 不同共病患者院外MACCE发生情况

对出院患者进行随访,随访中位时间12.6(12.3~13.0)个月,随访过程中因电话记录错误、拒绝随访等原因失访52人次,占比9.7%。随访1年

新发 MACCE 共 71 例人次，占比 13.4%（71/528），高 aCCI 组患者新发 MACCE 风险明显升高（log-rank $P=0.000\ 2$；图 1）。

2.3 不同共病患者院外发生 MACCE 的相关性

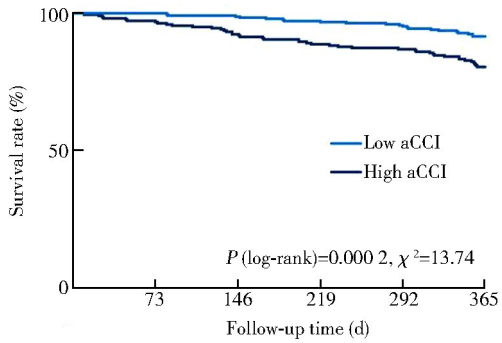
将 aCCI 划分为分类变量和连续变量，调整 GRACE 评分、NSTE-ACS 分类、cTNI、NT-proBNP、HB、eGFR、衰弱、多重用药、日常生活能力等混杂因素后，进行多因素 Cox 回归分析，若将 aCCI 作为连续变量，aCCI 每增加 1 个单位时，新发 MACCE 风险将增加 21.3%（$HR=1.213$，95% CI 1.043～1.412，$P=0.012$；图 2A）；若将 aCCI 作为分类变量，显示与低 aCCI 组相比，高 aCCI 组新发 MACCE 风险将增加85.8%（$HR=1.858$，95% CI 1.119～3.083，$P=0.017$；图 2B）。

表 1 老年 NSTE-ACS 患者人口学及临床特征

Table 1 Demographic and clinical characteristics of elderly patients with NSTE-ACS

Item	Low aCCI group ($n=277$)	High aCCI group ($n=251$)	Z/X^2	P value
Demographic data				
Age[years, $M(Q_1, Q_3)$]	69(67,73)	74(70,79)	−8.952	<0.001
Male[n(%)]	160(57.8)	148(59.0)	0.078	0.780
Smoking[n(%)]	123(44.4)	127(50.6)	2.026	0.155
Drinking[n(%)]	92(33.3)	90(36.0)	0.412	0.521
SBP[mmHg, $M(Q_1, Q_3)$]	133(122,143)	134(124,146)	−0.906	0.365
BMI[kg/m^2, $M(Q_1, Q_3)$]	23.3(23.4,27.8)	25.0(23.3,27.5)	−0.579	0.562
NSTEMI[n(%)]	18(6.5)	45(17.9)	16.372	<0.001
GRACE[$M(Q_1, Q_3)$]	116(106,125)	128(115,140)	−6.890	<0.001
Cardiac function classification[n(%)]			8.422	0.038
Ⅰ	137(49.5)	101(40.2)		
Ⅱ	128(46.2)	128(51.0)		
Ⅲ	10(3.6)	21(8.4)		
Ⅳ	2(0.7)	1(0.4)		
Laboratory test[$M(Q_1, Q_3)$]				
ALT(U/L)	14(12,20)	14(11,21)	−1.419	0.156
AST(U/L)	18.7(15.6,22.2)	18.1(15.2,22.5)	−0.617	0.537
ALB(g/L)	38.3(36.7,40.1)	37.6(35.9,39.8)	−1.917	0.055
eGFR[ml/(min · 1.73m^2)]	91.4(77.5,105.4)	82.2(67.3,97.0)	−4.946	<0.001
UA(μmol/L)	323.5(269.6,389.9)	343.2(284.4,407.8)	−2.328	0.020
TBIL(μmol/L)	13.6(10.5,17.0)	13.4(10.2,16.8)	−0.375	0.707
TC(mmol/L)	3.7(3.0,4.5)	3.7(3.1,4.5)	−0.299	0.765
TG(mmol/L)	1.3(1.0,1.8)	1.3(1.0,1.6)	−1.420	0.156
HDL-C(mmol/L)	1.0(0.9,1.2)	1.0(0.9,1.2)	−0.048	0.961
LDL-C(mmol/L)	2.0(1.7,2.6)	2.1(1.7,2.6)	−0.216	0.829
CK-MB(U/L)	1.0(0.7,1.6)	1.3(0.9,2.1)	−2.860	0.004
cTNI(U/L)	0.003(0.001,0.009)	0.005(0.002,0.018)	−3.672	<0.001
NT-proBNP(ng/L)	137(81,283)	272(110,748)	−5.932	<0.001
FGLU(mmol/L)	5.4(4.8,6.5)	6.0(5.0,7.9)	−4.071	<0.001
hs-CRP(mg/L)	1.0(0.4,2.8)	1.2(0.5,3.3)	−1.490	0.136
WBC(×10^9/L)	5.9(4.9,7.2)	6.1(5.2,7.2)	−1.163	0.245
HB(g/L)	133(124,144)	128(117,138)	−4.048	<0.001
PLT(×10^9/L)	194(166,233)	193(163,230)	−0.695	0.487
Echocardiography [$M(Q_1, Q_3)$]				
LA(cm)	3.78(3.50,4.00)	3.88(3.54,4.14)	−3.133	0.002
LVEDD(cm)	4.91(4.65,5.17)	4.98(4.64,5.30)	−1.670	0.095
LVESD(cm)	3.15(2.89,3.34)	3.21(2.96,3.54)	−3.302	<0.001
LVEF(%)	0.65(0.62,0.69)	0.64(0.60,0.67)	−4.600	<0.001
Comprehensive geriatric assessment[n(%)]				
Decline in BI	15(5.4)	39(15.5)	14.696	<0.001
Frailty	147(53.1)	187(74.5)	18.061	<0.001
Malnutrition or risk of malnutrition	46(16.6)	50(19.9)	0.972	0.324
Polypharmacy	96(34.7)	137(54.6)	21.203	<0.001
Sleep Disorders	18(6.5)	24(9.6)	1.688	0.194

NSTE-ACS: non-ST segment elevation acute coronary syndrome; aCCI: age-adjusted Charlson comorbidity index; SBP: systolic blood pressure; BMI: body mass index; NSTEMI: non-ST-segment elevation myocardial infarction; GRACE: global registry of acute coronary events; ALT: alanine aminotransferase; AST: aspartate aminotransferase; ALB: albumin; eGFR: estimated glomerular filtration rate; UA: uric acid; TBIL: total bilirubin; TC: total cholesterol; TG: triglyceride; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; CK-MB: creatine kinase-myocardial band; cTNI: cardiac troponin I; NT-proBNP: N-terminal pro-B-type natriuretic peptide; FGLU: fasting glucose; hs-CRP: high-sensitivity C-reactive protein; WBC: white blood cell; HB: hemoglobin; PLT: platelet; LA: left atrial diameter; LVEDD: left ventricular end-diastolic dimension; LVESD: left ventricular end-systolic dimension; LVEF: left ventricular ejection fraction; BI: Barthel index. 1 mmHg=0.133 kPa.



Follow-up time (d)	0	73	146	219	292	365
Low aCCI group (*n*)	253	253	251	246	242	230
High aCCI group (*n*)	223	215	208	198	194	175

图 1 老年 NSTE-ACS 患者院外未发生 MACCE 率比较

Figure 1 Comparison of post-discharge MACCE-free survival rates in older adults with NSTE-ACS

aCCI: adjusted Charlson comorbidity index; NSTE-ACS: non-ST segment elevation acute coronary syndrome; MACCE: major adverse cardiovascular and cerebrovascular events.

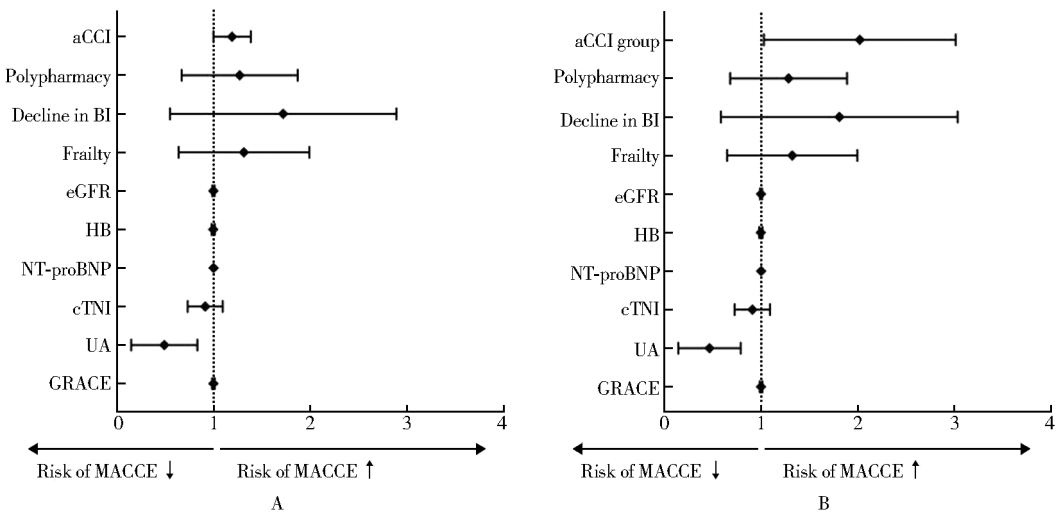


图 2 aCCI 与老年 NSTE-ACS 患者院外发生 MACCE 的相关性

Figure 2 Correlation between aCCI and post-discharge MACCE occurrence in older adults with NSTE-ACS

A: aCCI was included as a continuous variable in the multivariate Cox regression analysis; B: aCCI was set as a categorical variable based on high aCCI (aCCI≥5) and low aCCI (aCCI<5) and was included in the multivariate Cox regression analysis. aCCI: age-adjusted Charlson comorbidity index; NSTE-ACS: non-ST segment elevation acute coronary syndrome; MACCE: major adverse cardiovascular and cerebrovascular events; BI: Barthel index; eGFR: estimated glomerular filtration rate; HB: hemoglobin; NT-proBNP: N-terminal pro-B-type natriuretic peptide; cTNI: cardiac troponin I; UA: unstable angina; GRACE: global registry of acute coronary events.

3 讨 论

老年 NSTE-ACS 患病率逐年升高,此类患者有较高的不良事件风险[6]。既往研究发现,老年 NSTE-ACS 患者容易合并多种慢性疾病,增加不良预后[7]。患有两种及以上的慢性疾病称为共病,共病的老年 NSTE-ACS 患者容易出现全因死亡、跌倒和社会照护等情况[8]。本研究探讨共病与老年 NSTE-ACS 患者院外发生 MACCE 的关系,有望指导老年 NSTE-ACS 患者风险分层。

本研究发现老年 NSTE-ACS 合并高 aCCI 患者患病率 47.5%。国外研究发现,NSTE-ACS 合并共病的患病率为 38.7%~49.9%[9,10]。不同中心共病患病率略有不同,与纳入患者年龄及共病划分标准有关,但是此类患者共病患病率均较高。

本研究发现高 aCCI 组患者 NSTEMI 占比更大,GRACE 评分更高,此类患者尿酸水平更高,肌钙蛋白I、NT-proBNP 水平更高,而肌酐清除率及血红蛋白水平更低。国外多中心前瞻性队列研究纳入≥75岁 NSTE-ACS 患者,发现高共病患者 GRACE 评分更高,NSTEMI 占比更高,心功能分级更差,心肌损伤标志物及空腹血糖水平更高,出现血红蛋白、肌酐

清除率、肌酐等水平降低[11,12]，与本研究结果相一致。临床中对于共病患者进行整体化管理，制定适当营养方案，关注多器官功能，进行多器官康复，可改善预后。

本研究发现高 aCCI 组患者容易合并多种老年综合征。此类患者容易合并多种慢性疾病，它们具有相同发病机制，如氧化应激、慢性炎症反应及代谢障碍等。但多种老年综合征，如衰弱、肌少症等，上述机制也是其发病机制。共病与老年综合征具有交叉发病机制，两者相互作用，促进相互发生[13-15]，与本研究结果相一致。

本研究发现高 aCCI 组患者容易发生 MACCE，高 aCCI 是此类患者院外 MACCE 的独立危险因素。一项前瞻性队列研究纳入≥75 岁 NSTE-ACS 患者 704 例，CCI≥2 分患者的中风发生率（$P=0.005$）和死亡发生率（$P<0.001$）显著升高，并且发现 CCI 是老年 NSTE-ACS 患者院外 1 年全因死亡率的独立预测因子（$HR=1.632, 95\%CI\ 1.403\sim1.898; P<0.001$）[16]。以上研究与本研究结果一致。但是，本研究存在一定局限性，如样本量偏小、单中心研究、均为住院患者、随访时间较短等，使得本研究代表性不足。

综上，老年 NSTE-ACS 患者如何精准风险分层，给予个性化管理方案，减缓甚至阻断此类疾病对于老年人群不良事件的影响，始终是临床的热点问题。本研究发现 aCCI 与老年 NSTE-ACS 不良预后相关，为此类患者风险分层提供支撑，有利于科学管理老年NSTE-ACS 患者。

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