

## 缺血性心脏病合并消化道出血患者的住院死亡危险因素分析\*

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**【摘要】目的** 探讨缺血性心脏病(ischemic heart disease, IHD)合并消化道出血(gastrointestinal bleeding, GIB)患者发生住院死亡的危险因素。**方法** 纳入2015年1月-2018年1月在四川大学华西医院住院治疗的IHD合并GIB的患者,收集其一般资料、基础疾病史、既往抗凝抗血小板药物史、入院时实验室检查及住院治疗措施等资料。以住院期间死亡作为研究终点事件,通过多因素二元logistic回归等统计方法分析该类患者住院期间死亡的独立危险因素,绘制受试者操作特征(receiver operating characteristic, ROC)曲线并计算曲线下面积(area under curve, AUC)。**结果** 本研究共纳入符合标准的患者395例,其中342例患者好转出院,53例患者发生住院死亡事件,死因分析中心源性死亡居首位(54.7%),其次是感染性死亡(24.5%)。logistic回归分析结果显示ST段抬高型心肌梗死(ST-segment elevated myocardial infarction, STEMI)患者的死亡风险是非急性冠脉综合征患者的2.527倍[比值比(odds ratio, OR)=2.527, 95%置信区间(confidence interval, CI): 1.152~8.277, P=0.043],而合并慢性肾脏疾病患者的死亡风险是无肾脏疾病患者的2.89倍(OR=2.89, 95%CI: 1.187~7.037, P=0.019)。入院时较高的白细胞水平(OR=1.123, 95%CI: 1.057~1.193, P<0.001)和较低的血红蛋白水平(OR=1.014, 95%CI: 1.003~1.025, P=0.013)与患者住院死亡相关,而住院期间行内镜诊治(OR=0.305, 95%CI: 0.103~0.881, P=0.029)可降低患者的死亡风险。联合上述指标的ROC曲线,其预测患者发生住院死亡的AUC为0.79。**结论** IHD类型为STEMI、合并慢性肾脏疾病、入院时白细胞高和血红蛋白水平低,是IHD合并GIB的患者住院死亡结局的独立危险因素,而住院期间行内镜诊治是其保护因素。

**【关键词】** 缺血性心脏病 消化道出血 危险因素 住院死亡率

### Mortality Risk Factors for Inpatients with Ischemic Heart Disease Complicated with Gastrointestinal Bleeding

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**【Abstract】 Objective** To investigate the risk factors of in-hospital mortality in patients with combined ischemic heart disease (IHD) and gastrointestinal bleeding (GIB). **Methods** Patients who were hospitalized and received treatment for IHD combined with GIB at West China Hospital, Sichuan University between Jan. 2015 and Jan. 2018 were included in the study. Information concerning their baseline data, comorbidities, history of anticoagulant and antiplatelet medication, laboratory data on admission, and in-hospital treatments was collected. In-hospital death of all causes was taken as the primary endpoint event of the study, and multivariate logistic regression analysis was conducted to identify the independent risk factors of mortality during their hospital stay for this specific type of patients. Then, receiver operating characteristic (ROC) curve was drawn and the area under curve (AUC) was calculated accordingly. **Results** A total of 395 patients met the enrollment criteria and were included in the study. Among them, 342 patients were discharged after their condition improved, and 53 patients died during hospitalization. Analysis of the cause of death revealed that cardiogenic death was the leading cause of death (54.7%), which was followed by infection-caused death (24.5%). Logistic regression analysis revealed that patients with ST-segment elevation myocardial infarction (STEMI) had a 2.527-fold risk of mortality compared with patients with non-acute coronary syndrome (odds ratio [OR]=2.527, 95% confidence interval [CI]: 1.152-8.277, P=0.043), and patients with comorbidity of chronic renal disease (CKD) had a 2.89-fold risk of mortality (OR=2.89, 95%CI: 1.187-7.037, P=0.019). It was also shown the higher level of WBC count (OR=1.123, 95%CI: 1.057-1.193, P<0.001) and lower hemoglobin (OR=1.014, 95%CI: 1.003-1.025, P=0.013) on admission were related to in-hospital mortality. On the other hand, endoscopy (OR=0.305, 95%CI: 0.103-0.881, P=0.029) was identified as a protective factor in hospital treatment that decreased the risk of in-hospital mortality. ROC curve was drawn by combining the aforementioned variables to predict in-hospital mortality, which had an AUC of 0.79. **Conclusion** The actual type of IHD being STEMI, the patient's condition being complicated with chronic kidney disease, and having high white blood cells and low hemoglobin levels upon admission were considered independent risk

\* 四川省科技计划(No. 2019YJ0102)和四川大学华西医院学科卓越发展1.3.5工程临床研究孵化项目(No. 2020HXXFH039, No. 2020HXXFH054)资助

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factors for in-hospital death outcome of IHD patients complicated with GIB, while undergoing endoscopy during hospitalization was considered as a protective factor.

**【Key words】** Ischemic heart disease    Gastrointestinal bleeding    Risk factors    In-hospital mortality

缺血性心脏病(ischemic heart disease, IHD)是以心肌缺血为特征的一组临床疾病,分为急性冠状动脉综合征(acute coronary syndrome, ACS)和非急性冠状动脉综合征,其共同机制是冠状动脉部分或完全血栓闭塞所致的血液供需失衡<sup>[1]</sup>。IHD作为全球首要死亡原因,严重威胁人类的健康<sup>[1-2]</sup>。临床指南推荐抗血小板药作为IHD原发和复发性心血管事件的标准预防和治疗用药,但该治疗可增加患者消化道出血(gastrointestinal bleeding, GIB)的风险<sup>[3-5]</sup>,严重者可因活动性消化道大出血而死亡。然而GIB时机体因低血容量及代偿机制的作用,心血管事件的发生率亦将升高,从而增加住院死亡风险<sup>[6]</sup>。

IHD患者在发生GIB后往往急诊收入消化内科或心脏内科,临床工作中对该类患者的治疗棘手。无论是停用或恢复抗血小板药的时机,还是输血策略及内镜诊疗的时机,都需要充分权衡GIB与心血管事件发生风险的利弊。目前尚未完全明确影响此类患者住院死亡的危险因素,因此本研究回顾性分析了四川大学华西医院IHD患者发生GIB后入院的临床资料,以探讨此类患者住院死亡相关的危险因素。

## 1 材料与方法

### 1.1 研究对象

本研究回顾性分析了2015年1月–2018年1月在四川大学华西医院住院治疗的IHD合并GIB的患者资料。纳入标准(同时满足):①患者年龄>18岁;②明确诊断IHD(ICD-10编码: I20.0, 不稳定心绞痛; I21, 急性心肌梗塞; I25.1, 冠状动脉粥样硬化性心脏病; I25.2, 陈旧性心肌梗死);③入院时存在明确GIB(ICD-10编码: K92.0, 呕血; K92.1, 黑便; K92.2, 消化道出血, 未特指)。排除标准(至少满足其一):①临床资料不完善者;②O型Rh阴性血患者;③GIB与外伤或外科手术相关;④合并消化道恶性肿瘤者;⑤合并血液系统肿瘤或全身性血液系统疾病致凝血功能障碍者。

本研究已获得四川大学华西医院生物医学伦理委员会审核批准(2020年审496号),并于中国临床试验注册中心完成注册(注册号ChiCTR2000038169)。

### 1.2 研究方法

**1.2.1 数据收集** 通过四川大学华西医院数字化信息系统收集患者的临床资料,包括年龄、性别、吸烟饮酒史、

既往冠脉支架植入史、抗凝抗血小板药物使用史。基础疾病史包括高血压、糖尿病、慢性阻塞性肺疾病(chronic obstructive pulmonary disease, COPD)、慢性肾脏疾病(chronic kidney disease, CKD)、肝硬化、脑梗塞等。

入院实验室指标包括血红蛋白(hemoglobin, Hb)、白细胞计数(white blood cell, WBC)、血小板、白蛋白、总胆红素、血肌酐(serum creatinine, Scr)、尿素氮(blood urea nitrogen, BUN)、凝血酶原时间(prothrombin time, PT)、活化部分凝血活酶时间(activated partial thromboplastin time, APTT)、国际标准化比值(international normalized ratio, INR)、肌钙蛋白(troponin T, TnT)、肌酸激酶(creatine kinase-MB, CK-MB)、脑尿钠肽(brain natriuretic peptide, BNP)。住院期间治疗措施包括红细胞悬液输注、经皮冠状动脉介入治疗(percutaneous transluminal coronary intervention, PCI)及消化内镜诊治。

**1.2.2 住院结局相关定义** 研究主要终点为住院期间全因死亡事件,患者死因分为4大类:①心源性:心肌梗死、恶性心律失常、心力衰竭、心脏破裂、心源性猝死;②失血性:失血性休克;③感染性:全身各不同部位细菌所致感染性休克、脓毒血症;④其他原因:如急慢性肾功能衰竭、脑出血、脑梗死等。

### 1.3 统计学方法

定性资料以频率和百分比表示,采用卡方检验或Fisher确切概率法分析。定量资料均行正态性检验,对符合正态分布的连续变量以 $\bar{x} \pm s$ 描述,使用独立样本 $t$ 检验进行比较;对不服从正态分布的变量以中位数及四分位间距描述,采用Mann-Whitney  $U$ 检验。取单因素分析中差异有统计学意义的指标绘制受试者操作特征(receiver operating characteristic, ROC)曲线并计算曲线下面积(area under curve, AUC),筛选变量纳入logistic回归模型以探究住院死亡的危险因素,联合logistic回归分析中有统计学意义的指标绘制ROC曲线以预测患者的住院死亡风险。 $P < 0.05$ 为差异有统计学意义。

## 2 结果

### 2.1 存活组与死亡组患者一般资料比较

结果见表1。研究共纳入395例IHD合并GIB的住院患者,其中342例(86.6%)患者好转出院,53例(13.4%)发生住院死亡事件,死因分析显示心源性死亡29例(54.7%),

表 1 IHD合并GIB患者基本情况  
Table 1 Baseline data of patients with IHD and GIB

| Variable                        | Total (n=395) | Death (n=53) | Survival (n=342) | P      |
|---------------------------------|---------------|--------------|------------------|--------|
| Age/yr., $\bar{x} \pm s$        | 71.88±10.32   | 74.23±9.83   | 71.52±10.36      | 0.075  |
| Male/case (%)                   | 256 (64.8)    | 37 (69.8)    | 219 (64.0)       | 0.413  |
| Shock index ( $\bar{x} \pm s$ ) | 0.720±0.224   | 0.765±0.245  | 0.713±0.219      | 0.117  |
| Smoking/case (%)                | 180 (45.6)    | 25 (47.2)    | 155 (45.3)       | 0.802  |
| Alcohol/case (%)                | 99 (25.1)     | 13 (24.5)    | 86 (25.1)        | 0.923  |
| GIB history/case (%)            | 107 (27.1)    | 10 (18.9)    | 97 (28.4)        | 0.148  |
| Coronary stenting/case (%)      | 110 (27.8)    | 11 (20.8)    | 99 (28.9)        | 0.251  |
| Antiplatelet drug/case (%)      | 268 (67.8)    | 33 (62.3)    | 235 (68.7)       | 0.350  |
| Anticoagulation/case (%)        | 25 (6.3)      | 7 (13.2)     | 18 (5.3)         | 0.061  |
| Comorbidities/case (%)          |               |              |                  |        |
| Hypertension                    | 283 (71.6)    | 36 (67.9)    | 247 (72.2)       | 0.518  |
| Diabetes mellitus               | 147 (37.2)    | 17 (32.1)    | 129 (37.7)       | 0.428  |
| CKD <sup>a</sup>                | 95 (24.1)     | 28 (52.8)    | 67 (19.6)        | <0.001 |
| COPD                            | 36 (9.1)      | 8 (15.1)     | 28 (8.2)         | 0.121  |
| Cerebral infarction             | 59 (14.9)     | 8 (15.1)     | 50 (14.6)        | 0.928  |
| Cirrhosis                       | 25 (6.3)      | 3 (5.7)      | 22 (6.4)         | 0.561  |
| IHD category/case (%)           |               |              |                  | <0.001 |
| N-ACS                           | 213 (53.9)    | 21 (39.6)    | 192 (56.1)       |        |
| STEMI                           | 71 (18.0)     | 20 (37.7)    | 51 (14.9)        |        |
| N-STEMI                         | 52 (13.2)     | 8 (15.1)     | 44 (12.9)        |        |
| UA                              | 59 (14.9)     | 4 (7.6)      | 55 (16.1)        |        |
| Symptoms of GIB/case (%)        |               |              |                  | 0.546  |
| Hematemesis                     | 105 (26.6)    | 12 (22.6)    | 93 (27.2)        |        |
| Melena                          | 226 (57.2)    | 34 (64.2)    | 192 (56.1)       |        |
| Hematochezia                    | 64 (16.2)     | 7 (13.2)     | 57 (16.7)        |        |

IHD: Ischemic heart disease; GIB: Gastrointestinal bleeding; CKD: Chronic renal disease; COPD: Chronic obstructive pulmonary disease; N-ACS: Non-acute coronary syndrome; STEMI: ST-segment elevated myocardial infarction; N-STEMI: Non-ST segment elevated myocardial infarction; UA: Unstable angina; a: CKD included stage of G3 (eGFR 30-59 mL/[min·1.73 m<sup>2</sup>]), G4 (eGFR 15-29 mL/[min·1.73 m<sup>2</sup>]) and G5 (eGFR<15 mL/[min·1.73 m<sup>2</sup>]).

感染性死亡13例(24.5%),失血性死亡5例(9.4%),其他原因死亡6例(3例终末期肾衰竭,1例脑梗死,1例急性延髓出血,1例多器官功能衰竭)。

两组患者年龄、性别、既往抗凝抗血小板药物使用史等差异均无统计学意义。基础性疾病分析显示高血压与糖尿病作为患者最常见合并症,占比于两组间无明显差异( $P>0.05$ ),但死亡组患者中既往合并CKD者多于存活组( $P<0.001$ )。

所有患者中主要消化道出血症状为黑便(57.2%),且两组间症状构成无明显差异( $P=0.546$ )。所有患者中IHD类型以非急性冠脉综合征(53.9%)为主,但死亡组中ST段抬高型心梗(ST-segment elevated myocardial infarction, STEMI)患者更多,两组患者间IHD类型构成比差异有统计学意义( $P<0.001$ )。

## 2.2 存活组与死亡组患者入院实验室检查及住院治疗比较

如表2所示,死亡组患者入院时Hb水平较低,而WBC高于存活组,两者差异均有统计学意义( $P<0.001$ ),且死亡组患者死亡前Hb水平低于入院时水平[(82.34±27.95) g/L vs. (91.84±30.12) g/L,  $P<0.001$ ]。生化和凝血指标示死亡组患者入院时Scr水平更高( $P<0.001$ ),APTT更长( $P=0.038$ ),且入院时死亡组患者的心脏功能更差,其CK-MB、BNP及TnT含量均高于存活组患者( $P<0.01$ )。两组患者间血小板、白蛋白、BUN、PT、INR等差异均无统计学意义。住院期间共172例(43.5%)患者行红细胞悬液输注,74例(18.7%)患者接受了PCI,尽管死亡组中有更多患者接受了输血治疗和PCI治疗,但两组间差异并无统计学意义;与此同时,存活组中更多患者接受了消化内镜的诊治( $P<0.001$ )。

2.3 住院死亡相关危险因素分析

2.3.1 单因素ROC曲线绘制 取单因素分析结果中有统计学意义的指标(消化内镜诊治、IHD类别、合并CKD, 入院时Hb、WBC、Scr、APTT、CK-MB、BNP及TnT), 预测是否发生住院死亡, 绘制ROC曲线并计算相应AUC(图1)。结果显示TnT的AUC为0.732[95%置信区间(confidence interval, CI): 0.685 ~ 0.775,  $P < 0.000\ 1$ ], CK-MB的AUC为0.712(95%CI: 0.665 ~ 0.757,  $P < 0.000\ 1$ ), 入院时WBC的

表 2 IHD合并GIB患者入院实验室检查及住院治疗资料  
Table 2 Laboratory data on admission and in-hospital treatments for patients with IHD and GIB

| Variable                                                      | Total (n=395)         | Death (n=53)             | Survival (n=342)      | P      |
|---------------------------------------------------------------|-----------------------|--------------------------|-----------------------|--------|
| Laboratory data on admission                                  |                       |                          |                       |        |
| Hb/(g/L), $\bar{x} \pm s$                                     | 94.08±30.73           | 91.84±30.12              | 108.55±30.97          | <0.001 |
| WBC/( $\times 10^9\ L^{-1}$ ), $\bar{x} \pm s$                | 9.20±4.81             | 12.34±6.50               | 8.71±4.28             | <0.001 |
| Platelet/( $\times 10^9\ L^{-1}$ ), $\bar{x} \pm s$           | 177.70±93.10          | 187.79±88.49             | 175.61±95.77          | 0.376  |
| Albumin/(g/L), $\bar{x} \pm s$                                | 35.60±6.41            | 34.78±5.93               | 35.72±6.47            | 0.321  |
| Total bilirubin/( $\mu\text{mol/L}$ ), M ( $P_{25}, P_{75}$ ) | 9.85 (6.77, 16.48)    | 9.50 (6.75, 17.55)       | 9.95 (6.70, 16.43)    | 0.858  |
| Scr/( $\mu\text{mol/L}$ ), M ( $P_{25}, P_{75}$ )             | 98.00 (74.00, 158.00) | 129.00 (96.00, 249.50)   | 95.00 (72.75, 148.00) | <0.001 |
| BUN/(mmol/L), M ( $P_{25}, P_{75}$ )                          | 9.79 (6.40, 16.57)    | 11.57 (7.21, 18.14)      | 9.30 (6.16, 16.23)    | 0.096  |
| PT/s, M ( $P_{25}, P_{75}$ )                                  | 12.50 (11.70, 13.60)  | 13.00 (11.90, 14.75)     | 12.45 (11.70, 13.48)  | 0.360  |
| APTT/s, M ( $P_{25}, P_{75}$ )                                | 28.60 (25.30, 33.00)  | 30.50 (26.10, 39.10)     | 28.30 (25.20, 32.90)  | 0.038  |
| INR (M [ $P_{25}, P_{75}$ ])                                  | 1.09 (1.02, 1.19)     | 1.15 (1.01, 1.28)        | 1.09 (1.02, 1.17)     | 0.158  |
| CK-MB/(ng/mL), M ( $P_{25}, P_{75}$ )                         | 3.95 (1.76, 7.78)     | 6.28 (3.75, 13.14)       | 2.56 (1.61, 6.39)     | <0.001 |
| BNP/(ng/L), M ( $P_{25}, P_{75}$ )                            | 2 481 (678, 4 950)    | 5 330 (937, 13 535)      | 1 806 (592, 4 402)    | 0.002  |
| TnT/(ng/L), M ( $P_{25}, P_{75}$ )                            | 78.90 (19.50, 336.90) | 118.50 (61.40, 1 437.50) | 30.80 (13.50, 288.90) | <0.001 |
| In-hospital treatments/case (%)                               |                       |                          |                       |        |
| PCI                                                           | 74 (18.7)             | 14 (26.4)                | 60 (17.5)             | 0.124  |
| Transfusion                                                   | 172 (43.5)            | 29 (54.7)                | 143 (41.8)            | 0.078  |
| Endoscopy                                                     | 117 (29.6)            | 4 (7.5)                  | 113 (33.0)            | <0.001 |

Hb: Hemoglobin; WBC: White blood cell; Scr: Serum creatinine; BUN: Blood urea nitrogen; PT: Prothrombin time; APTT: Activated partial thromboplastin time; INR: International normalized ratio; CK-MB: Creatine kinase-MB; BNP: Brain natriuretic peptide; TnT: Troponin T; PCI: Percutaneous transluminal coronary intervention.

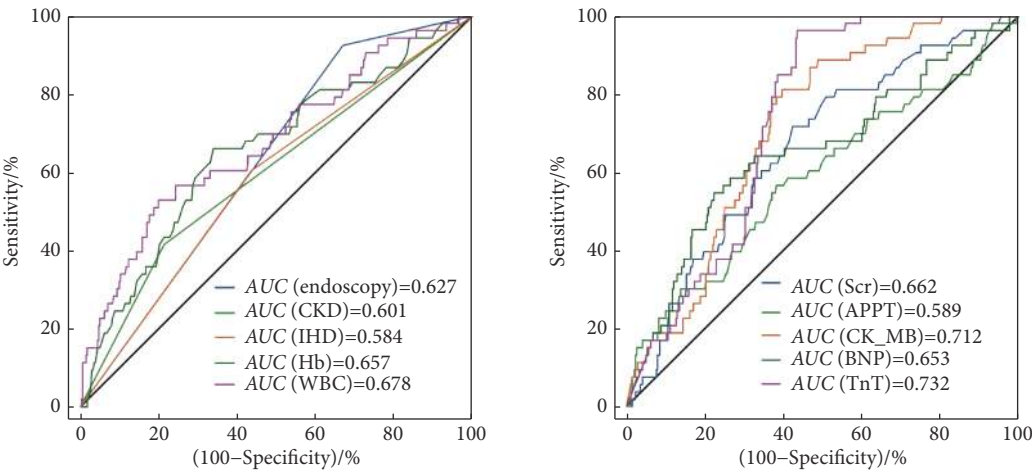


图 1 单因素指标预测住院死亡的ROC曲线

Fig 1 ROC curves for single-risk-factor prediction of in-hospital mortality

CKD, IHD, Hb, WBC, Scr, APTT, CK-MB, BNP, and TnT denote the same meaning as those in table 1 or table 2 did.

$AUC$ 为0.678(95%CI: 0.629 ~ 0.724,  $P < 0.0001$ ), Scr的 $AUC$ 为0.662(95%CI: 0.613 ~ 0.708,  $P < 0.0001$ ), Hb的 $AUC$ 为0.657(95%CI: 0.608 ~ 0.704,  $P = 0.0002$ ), BNP的 $AUC$ 为0.653(95%CI: 0.603 ~ 0.700,  $P = 0.0005$ ), 消化内镜诊治的 $AUC$ 为0.627(95%CI: 0.578 ~ 0.675,  $P < 0.0001$ ), 合并CKD的 $AUC$ 为0.601(95%CI: 0.551 ~ 0.649,  $P = 0.005$ ), IHD类别的 $AUC$ 为0.584(95%CI: 0.534 ~ 0.633,  $P = 0.0212$ ), APTT的 $AUC$ 为0.589(95%CI: 0.538 ~ 0.638,  $P = 0.0503$ )。

**2.3.2 多因素二元logistic回归分析** 将消化内镜诊治、IHD类别、合并CKD、入院时Hb、WBC、Scr、CK-MB、BNP及TnT作为协变量纳入多因素二元logistic回归模型以探索死亡相关危险因素。回归分析结果如表3所示, STEMI患者的住院死亡风险是非急性冠脉综合征患者的2.527倍[比值比(odds ratio, OR) = 2.527, 95%CI: 1.152 ~ 8.277,  $P = 0.043$ ], 而CKD患者的死亡风险是无肾脏并发症患者的2.890倍(OR = 2.890, 95%CI: 1.187 ~ 7.037,  $P = 0.019$ )。入院时较高的WBC水平(OR = 1.123, 95%CI: 1.057 ~ 1.193,  $P < 0.001$ )和较低的Hb水平(OR = 1.014, 95%CI: 1.003 ~ 1.025,  $P = 0.013$ )是患者住院死亡的独立危险因素。与此同时, 住院期间行消化内镜诊治(OR = 0.305, 95%CI: 0.103 ~ 0.881,  $P = 0.029$ )作为保护性因素, 可降低患者的住院死亡风险。

表3 住院期间死亡相关危险因素多变量logistic回归分析

Table 3 Multivariable logistic regression analysis of risk factors associated with mortality

| Variable             | OR    | 95% CI      | P      |
|----------------------|-------|-------------|--------|
| Endoscopy (no)       |       |             |        |
| Yes                  | 0.305 | 0.103-0.881 | 0.029  |
| IHD category (N-ACS) |       |             |        |
| STEMI                | 2.527 | 1.152-8.277 | 0.043  |
| N-STEMI              | 2.600 | 0.704-9.597 | 0.152  |
| UA                   | 1.686 | 0.428-6.645 | 0.455  |
| CKD (no)             |       |             |        |
| Yes                  | 2.890 | 1.187-7.037 | 0.019  |
| Scr                  | 0.999 | 0.996-1.001 | 0.337  |
| Hb                   | 1.014 | 1.003-1.025 | 0.013  |
| WBC                  | 1.123 | 1.057-1.193 | <0.001 |
| CK-MB                | 1.003 | 0.973-1.091 | 0.432  |
| BNP                  | 1.000 | 0.999-1.001 | 0.525  |
| TnT                  | 0.999 | 0.990-1.001 | 0.433  |

IHD, N-ACS, STEMI, N-STEMI, UA, CKD, Scr, Hb, WBC, CK-MB, BNP, TnT: Denote the same as those in table 1 or table 2. OR: Odds ratio; CI: Confidence interval.

联合消化内镜诊治、IHD类型、合并CKD、入院时Hb及WBC水平绘制ROC曲线(图2), 结果示联合模型预测患者住院死亡的 $AUC$ 为0.79(95%CI: 0.746 ~ 0.829,  $P < 0.001$ )。

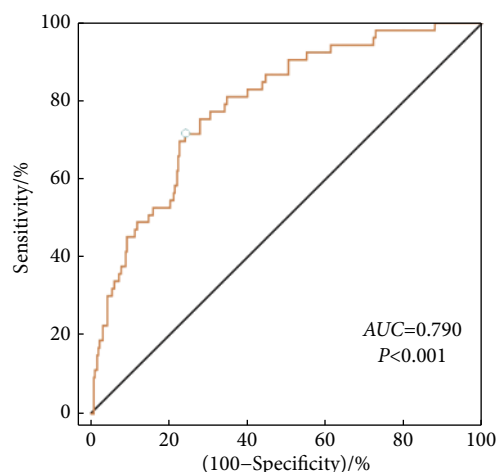


图2 多因素联合指标预测住院死亡的ROC曲线

Fig 2 ROC curve predicting in-hospital mortality with combined multiple risk factors

### 3 讨论

IHD与GIB均为临床常见危急重症, 同时罹患两种疾病时患者的短期死亡风险明显增高, 然而此类特殊患者住院期间的死亡相关危险因素目前并未十分明确。因单因素ROC曲线的指标预测住院死亡风险的效能不高, 故本研究行多因素二元logistic回归模型筛选死亡相关危险因素。本研究发现STEMI、合并CKD、入院时较高的WBC水平及较低的Hb含量是IHD合并GIB患者发生住院死亡的独立危险因素, 而住院期间行消化内镜诊治可降低患者的住院死亡风险。本研究进一步用筛选出来的死亡相关危险因素绘制联合预测的ROC曲线, 发现 $AUC$ 仅为0.79, 预测效能不高, 提示联合模型尚不能用于临床预测患者住院死亡。

既往研究报道GIB患者30 d内住院死亡率约为2.54%, 急性心梗患者为4.35%<sup>[7]</sup>。本研究中同时罹患两种疾病的患者住院死亡率升至13.4%, 提示IHD患者发生GIB意味着较高的住院死亡风险。研究表明急性心梗合并GIB患者住院死亡率为24.7%<sup>[8]</sup>, 高于本研究中患者住院死亡率, 可能是由于本研究中患者IHD类型多为非急性冠脉综合征, 回归分析结果也显示STEMI患者的住院死亡风险是非急性冠脉综合征患者的2.527倍, 故稳定性IHD患者合并GIB的死亡风险相对较低。同时本研究中患者住院死因以心源性为主, 同既往研究一致<sup>[9]</sup>, 提示住院期间应尤为重视此类患者的IHD病情变化。

CKD作为IHD的主要危险因素之一<sup>[10]</sup>,有研究发现不同程度的肾功能不全与ACS患者的死亡风险升高有关<sup>[11]</sup>。并且轻-中度肾功能不全也与住院期间GIB密切相关<sup>[12]</sup>,既往Meta分析报道GIB患者合并CKD的死亡风险是未合并CKD者的1.78倍,而合并终末期肾病的死亡风险是未合并者的2.5倍<sup>[13]</sup>。本研究进一步证实了CKD可作为IHD合并GIB患者住院死亡的独立危险因素( $OR=2.890$ ),在临床工作中需及早识别此类高危患者,以改善患者的不良预后。

WBC计数作为反映机体抗感染及炎症状态的重要指标之一,既往研究报道WBC水平是IHD合并GIB患者住院死亡相关的危险因素<sup>[8]</sup>,本研究结果与之一致。机体感染状态下应激性溃疡相关GIB的风险增加<sup>[14]</sup>,一旦发生GIB,黏膜屏障受损更易出现肠道细菌感染,两者互相促进,形成恶性循环<sup>[15]</sup>。与此同时,感染炎症可破坏冠脉粥样硬化斑块的稳定性而加重心肌缺血,也可影响心脏传导系统,进而诱发各类心律失常,增加住院患者短期死亡风险。STEMI患者住院发生重大感染的短期死亡风险是未发生感染者的3~5倍<sup>[16]</sup>。本研究中患者的次要死因是感染性休克与脓毒血症,也证实了感染是影响IHD合并GIB患者死亡的重要因素。

住院期间相应专科治疗是影响患者住院死亡率的另一重要因素。消化内镜作为GIB的关键诊疗措施,尽管既往多篇研究已表明IHD合并GIB的患者接受内镜检查与治疗是安全的<sup>[17-18]</sup>,但本研究中死亡组患者更少接受消化内镜诊治,这可能是由于临床医生高估了IHD患者行内镜检查的相关风险,如心肌梗死、恶性心律失常等。指南建议对急性上消化道出血的患者行早期内镜检查(出血后24 h内),而对于有严重合并症如IHD的患者,内镜检查的确切时机仍不明确<sup>[19]</sup>。本研究结果显示内镜作为患者住院死亡的保护因素,可降低住院死亡风险,因此对于此类患者,内镜检查及治疗在多学科治疗中应该处于更加积极的地位。

对于GIB,指南建议采用限制性输血策略<sup>[20-21]</sup>,但对于IHD合并GIB的患者,限制性输血的阈值(80 g/L)被认为并不恰当,其会增加患者的死亡率<sup>[22]</sup>。国际共识小组也认为较高的Hb浓度对IHD患者是有益的<sup>[19]</sup>,但适当的输血阈值仍不清楚。本研究也发现较低的Hb浓度是住院死亡率的独立危险因素。因此当发生GIB时,应考虑限制性输血策略,但对于IHD患者,较高的输血阈值可能更合适,最佳的输血阈值尚有待前瞻性研究加以明确。

本研究亦存在一定局限性。首先,这是一项单中心回顾性研究,不可避免地存在选择偏倚和信息偏倚;其

次,样本量仅纳入395例患者,未来需要开展多中心、大样本的前瞻性队列研究以进一步探索和验证。尽管存在这些局限性,但本研究明确了此类患者的住院死亡相关危险因素,了解这些危险因素可以辅助临床医生早期识别高危患者,为改善患者预后的临床管理提供了依据。

\* \* \*

**利益冲突** 所有作者均声明不存在利益冲突

## 参 考 文 献

- [1] GBD 2019 Diseases and Injuries Collaborators. Global burden of 369 diseases and injuries in 204 countries and territories, 1990–2019: A systematic analysis for the Global Burden of Disease Study 2019. *Lancet*, 2020, 396(10258): 1204–1222.
- [2] 张干深, 宇传华, 罗丽莎, 等. 1990–2015年中国缺血性心脏病疾病负担趋势分析. *中华预防医学杂志*, 2017, 51(10): 915–921.
- [3] LANAS Á, CARRERA-LASFUENTES P, ARGUEDAS Y, *et al.* Risk of upper and lower gastrointestinal bleeding in patients taking nonsteroidal anti-inflammatory drugs, antiplatelet agents, or anticoagulants. *Clin Gastroenterol Hepatol*, 2015, 13(5): 906–912.
- [4] KAWASAKI K, KURAHARA K, YANAI S, *et al.* Low-dose aspirin and non-steroidal anti-inflammatory drugs increase the risk of bleeding in patients with gastroduodenal ulcer. *Dig Dis Sci*, 2015, 60(4): 1010–1015.
- [5] ALBEIRUTI R, CHAUDHARY F, ALQAHTANI F, *et al.* Incidence, predictors, and outcomes of gastrointestinal bleeding in patients admitted with ST-elevation myocardial infarction. *Am J Cardiol*, 2019, 124(3): 343–348.
- [6] KYAW M H, CHAN F K L. Managing antithrombotic agents in the setting of acute gastrointestinal bleeding. *Gastrointest Endosc Clin N Am*, 2018, 28(3): 351–361.
- [7] WILCOX C M, CRYER B L, HENK H J, *et al.* Mortality associated with gastrointestinal bleeding events: Comparing short-term clinical outcomes of patients hospitalized for upper GI bleeding and acute myocardial infarction in a US managed care setting. *Clin Exp Gastroenterol*, 2009, 2: 21–30.
- [8] HE L, ZHANG J, ZHANG S. Risk factors of in-hospital mortality among patients with upper gastrointestinal bleeding and acute myocardial infarction. *Saudi J Gastroenterol*, 2018, 24(3): 177–182.
- [9] WANG N, LI T, DU Q. Risk factors of upper gastrointestinal hemorrhage with acute coronary syndrome. *Am J Emerg Med*, 2019, 37(4): 615–619.
- [10] SARNAK M J, AMANN K, BANGALORE S, *et al.* Chronic kidney disease and coronary artery disease: JACC state-of-the-art review. *J Am Coll Cardiol*, 2019, 74(14): 1823–1838.
- [11] EL-MENYAR A, ZUBAID M, SULAIMAN K, *et al.* In-hospital major clinical outcomes in patients with chronic renal insufficiency presenting with acute coronary syndrome: data from a Registry of 8176 patients. *Mayo Clin Proc*, 2010, 85(4): 332–340.
- [12] ISHIGAMI J, GRAMS M E, NAIK R P, *et al.* Chronic kidney disease

- and risk for gastrointestinal bleeding in the Community: The Atherosclerosis Risk in Communities (ARIC) Study. *Clin J Am Soc Nephrol*, 2016, 11(10): 1735–1743.
- [13] HÁGENDORN R, FARKAS N, VINCZE Á, *et al.* Chronic kidney disease severely deteriorates the outcome of gastrointestinal bleeding: A meta-analysis. *World J Gastroenterol*, 2017, 23(47): 8415–8425.
- [14] BARDOU M, QUENOT J P, BARKUN A. Stress-related mucosal disease in the critically ill patient. *Nat Rev Gastroenterol Hepatol*, 2015, 12(2): 98–107.
- [15] YANG Q Y, OUYANG J, YANG J D. Sepsis as an important risk factor for gastrointestinal bleeding in acute coronary syndrome patients: Two case reports. *Medicine (Baltimore)*, 2018, 97(36): e12273[2021-07-05]. [https://journals.lww.com/md-journal/Fulltext/2018/09070/Sepsis\\_as\\_an\\_important\\_risk\\_factor\\_for.110.aspx](https://journals.lww.com/md-journal/Fulltext/2018/09070/Sepsis_as_an_important_risk_factor_for.110.aspx). doi: 10.1097/MD.00000000012273.
- [16] NASH M C, STROM J A, PATHAK E B. Prevalence of major infections and adverse outcomes among hospitalized. ST-elevation myocardial infarction patients in Florida, 2006. *BMC Cardiovasc Disord*, 2011, 11: 69[2021-07-05]. <https://bmccardiovascdisord.biomedcentral.com/articles/10.1186/1471-2261-11-69>. doi: 10.1186/1471-2261-11-69.
- [17] SIDDIQUI M T, BILAL M, GOLLAPUDI L A, *et al.* Endoscopy is relatively safe in patients with acute ischemic stroke and gastrointestinal hemorrhage. *Dig Dis Sci*, 2019, 64(6): 1588–1598.
- [18] HOFFMAN G R, STEIN D J, MOORE M B, *et al.* Safety of endoscopy for hospitalized patients with acute myocardial infarction: A national analysis. *Am J Gastroenterol*, 2020, 115(3): 376–380.
- [19] BARKUN A N, ALMADI M, KUIPERS E J, *et al.* Management of nonvariceal upper gastrointestinal bleeding: Guideline recommendations from the International Consensus Group. *Ann Intern Med*, 2019, 171(11): 805–822.
- [20] SUNG J J, CHIU P W, CHAN F K L, *et al.* Asia-Pacific working group consensus on non-variceal upper gastrointestinal bleeding: An update 2018. *Gut*, 2018, 67(10): 1757–1768.
- [21] ODUTAYO A, DESBOROUGH M J, TRIVELLA M, *et al.* Restrictive versus liberal blood transfusion for gastrointestinal bleeding: A systematic review and meta-analysis of randomised controlled trials. *Lancet Gastroenterol Hepatol*, 2017, 2(5): 354–360.
- [22] WANG Y, SHI X, WEN M, *et al.* Restrictive versus liberal blood transfusion in patients with coronary artery disease: A meta-analysis. *Curr Med Res Opin*, 2017, 33(4): 761–768.
- (2021-07-24收稿, 2021-10-09修回)
- 编辑 余琳