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## 急性心肌梗死合并肺部感染患者多药耐药菌分布特征 及心肌酶谱指标与炎症因子的关系分析\*

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**摘要 目的:**分析急性心肌梗死合并肺部感染患者多药耐药菌分布特征及炎症因子与心肌酶谱指标的关系。**方法:**选择2015年2月~2018年10月期间中国人民解放军联勤保障部队第940医院收治的67例急性心肌梗死合并肺部感染患者作为感染组,选取同期收治的60例单纯急性心肌梗死患者作为未感染组,分析感染组多药耐药菌的分布及其耐药性,比较两组炎症因子与心肌酶谱指标水平,采用Pearson相关性分析感染组患者炎症因子与心肌酶谱指标的相关性。**结果:**67例患者痰培养标本中共分离出136株病原菌,其中有64株属于多药耐药菌,多药耐药菌中革兰阴性菌38株,占59.37%,革兰阳性菌26株,占40.63%。其中主要革兰阴性菌对哌拉西林/舒巴坦、头孢哌酮/舒巴坦、阿米卡星、美罗培南、亚胺培南等较为敏感,主要革兰阳性菌对替考拉宁、万古霉素、利福平等较为敏感。感染组患者白细胞介素-6(IL-6)、乳酸脱氢酶(LDH)、促血管生成素-2(Ang-2)、肌酸激酶(CK)、肿瘤坏死因子- $\alpha$ (TNF- $\alpha$ )、谷草转氨酶(AST)、肌酸激酶同工酶(CKMB)水平均高于未感染组患者( $P<0.05$ )。经Pearson相关性分析可得,感染组患者血清IL-6、Ang-2、TNF- $\alpha$ 水平与AST、LDH、CK、CK-MB水平均呈正相关( $P<0.05$ )。**结论:**急性心肌梗死合并肺部感染患者心肌酶谱与炎症因子水平关系密切,有助于判断患者病情严重程度,且急性心肌梗死合并肺部感染患者多药耐药现象较为严重,临床应针对病原菌合理选取抗菌药物。

**关键词:**肺部感染;心肌酶谱;急性心肌梗死;炎症因子;病原菌;耐药

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## Distribution Characteristics of Multidrug-resistant Bacteria in Patients with Acute Myocardial Infarction Complicated with Pulmonary Infection and the Relationship between Myocardial Enzymes and Inflammatory Factors\*

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**ABSTRACT Objective:** To analyze the distribution of multidrug-resistant bacteria in patients with acute myocardial infarction complicated with pulmonary infection and the relationship between inflammatory factors and myocardial enzymes. **Methods:** 67 patients with acute myocardial infarction complicated with pulmonary infection who were admitted to 940 Hospital of PLA Joint Logistics Support Force from February 2015 to October 2018 were selected as infection group, and 60 patients with simple myocardial infarction who were admitted in the same period were selected as uninfected group. The distribution and drug resistance of multidrug-resistant bacteria in infection group were analyzed. The levels of inflammatory factors and myocardial enzymes were compared between the two groups. Pearson correlation was used to analyze the correlation between inflammatory factors and myocardial enzymes in patients with infection group. **Results:** A total of 136 pathogenic bacteria were isolated from sputum culture specimens of 67 patients. Among them, 64 strains belong to multi-drug resistant bacteria, 38 strains of Gram-negative bacteria account for 59.37%, 26 strains of Gram-positive bacteria account for 40.63%. Gram-negative bacteria were more sensitive to piperacillin/sulbactam, cefoperazone/sulbactam, amikacin, meropenem and imipenem. Gram-positive bacteria were sensitive to teicoplanin, vancomycin and rifampicin. The levels of interleukin-6 (IL-6), lactate dehydrogenase (LDH), angiopoietin-2 (Ang-2), creatine kinase (CK), tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), aspartate aminotransferase (AST), creatine kinase isoenzyme (CKMB) in the infected group were higher than those in the uninfected group ( $P<0.05$ ). According to Pearson correlation analysis, the serum levels of IL-6, Ang-2 and TNF- $\alpha$  were positively correlated with the levels of AST, LDH, CK and CK-MB ( $P<0.05$ ). **Conclusion:** Myocardial enzymes of patients with acute myocardial infarction complicated with pulmonary infection is closely related to the level of inflammatory factors, which is helpful to judge the severity of patients' condition.

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Meanwhile, multidrug resistance in patients with acute myocardial infarction complicated with pulmonary infection is more serious, and antibiotics should be reasonably selected according to pathogenic bacteria in clinic.

**Key words:** Pulmonary infection; Acute myocardial enzymes; Myocardial infarction; Inflammatory factors; Pathogenic bacteria; Drug resistance

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## 前言

急性心肌梗死是心内科常见危急重症之一,是由冠状动脉急性、持续性缺血缺血所引起的心肌坏死,同时伴有血清心肌酶活性升高及心电图产生进行性变化,可并发休克、心律失常以及心力衰竭等,致残率、致死率较高<sup>[1-3]</sup>。该类患者一经确诊,需要立即住院给予相关治疗以防休克、心律失常以及心力衰竭等并发症发生<sup>[4-5]</sup>。但在治疗过程中,临床上发现部分患者在住院期间常引发肺部感染,影响患者预后。因此,了解常见病原菌的分布及合理使用抗菌药物,可有效降低该类疾病的病死率<sup>[6-8]</sup>。同时,已有不少研究发现急性心肌梗死合并肺部感染患者体内炎性因子有异常升高的现象<sup>[9,10]</sup>。鉴于此,本研究通过探讨急性心肌梗死合并肺部感染患者多药耐药菌分布特征及炎性因子与心肌酶谱指标的关系,以期为临床提供参考。

## 1 资料和方法

### 1.1 临床资料

选择 2015 年 2 月~2018 年 10 月期间中国人民解放军勤保障部队第 940 医院收治的 67 例急性心肌梗死合并肺部感染患者作为感染组,选取同期收治的 60 例单纯急性心肌梗死患者作为未感染组。纳入标准:(1)急性心肌梗死符合《急性心肌梗死诊断和治疗指南》(2001 版本)<sup>[11]</sup>中的相关诊断标准;(2)患者及其家属知情本次研究并已签署知情同意书;(3)肺部感染诊断依据:临床症状、体征及胸部 X 线。排除标准:(1)合并其他炎症性疾病者;(2)合并其他恶性肿瘤者;(3)合并免疫系统疾病者。其中感染组男 37 例,女 30 例,年龄 42~68 岁,平均(54.61±3.09)岁;未感染组男 32 例,女 28 例,年龄 41~69 岁,平均(55.29±4.95)岁。两组患者一般资料比较无差异( $P>0.05$ ),均衡可比。

### 1.2 方法

**1.2.1 血标本采集** 抽取所有研究对象清晨空腹静脉血 5ml,以 2500 r/min 离心 8 min,分离血清,置于 -20℃ 冰箱中待测。采用酶联免疫吸附试验检测白细胞介素 -6(Interleukin-6, IL-6)、促血管生成素 -2(Angiopoietin-2, Ang-2)以及肿瘤坏死因子 - $\alpha$ (Tumor necrosis factor- $\alpha$ , TNF- $\alpha$ )水平,试剂盒购自上海晶都生物技术有限公司,严格遵守试剂盒说明书进行。采用日本 OLYMPUS-AU600 型全自动生化分析仪检测血清乳酸脱氢酶(Lactate dehydrogenase, LDH)、谷草转氨酶(Glutamic oxaloacetic transaminase, AST)、肌酸激酶同工酶(Creatine kinase isoenzyme, CKMB)、肌酸激酶(Creatine kinase, CK)水平。

**1.2.2 标本采集、菌株鉴定以及药敏试验** 感染组患者清晨用清水漱口 3 次后,用力咳出呼吸道深部痰液至无菌广口瓶内,采集不少于 1 mL 的痰标本,采用美国 BD 公司生产的 Sceptor

细菌鉴定仪进行药敏试验,试纸条购自上海飞测生物科技有限公司。

### 1.3 统计学方法

研究数据采用 SPSS25.0 软件进行分析,计量资料用均数±标准差( $\bar{x}\pm s$ )描述,采用  $t$  检验,计数资料用%描述,两组比较采用  $\chi^2$  检验,采用 Pearson 相关性分析炎性因子与心肌酶谱指标的相关性, $P<0.05$  认为差异有统计学意义。

## 2 结果

### 2.1 感染组患者多药耐药菌分布

67 例感染组患者痰培养标本中共分离出 136 株病原菌,其中有 64 株属于多药耐药菌,多药耐药菌中革兰阳性菌占 40.63%(26/64),革兰阴性菌占 59.37%(38/64),见表 1。

表 1 感染组患者多药耐药菌分布及构成比(%)

Table 1 Distribution and composition ratio of multidrug-resistant bacteria in infected patients(%)

Pathogenic bacteria	n	Composition ratio
Gram-negative bacteria	38	59.37
<i>Klebsiella pneumoniae</i>	16	25.00
<i>Escherichia coli</i>	9	14.06
<i>Acinetobacter baumannii</i>	6	9.37
<i>Haemophilus influenzae</i>	2	3.13
<i>Pseudomonas aeruginosa</i>	2	3.13
<i>Enterobacter cloacae</i>	1	1.56
Proteus	1	1.56
Other	1	1.56
Gram-positive bacteria	26	40.63
<i>Streptococcus pneumoniae</i>	13	20.31
<i>Staphylococcus aureus</i>	8	12.50
Enterococcus	2	3.13
<i>Staphylococcus epidermidis</i>	2	3.13
Other	1	1.56
Total	64	100.00

### 2.2 主要革兰阴性菌对抗菌药物的耐药性

主要革兰阴性菌对青霉素类、环丙沙星、左氧氟沙星、头孢菌素、庆大霉素等抗菌药物耐药率较高,部分可达 100.00%,大肠埃希菌、鲍氏不动杆菌对阿莫西林耐药率较高,而主要革兰阴性菌对哌拉西林/舒巴坦、头孢哌酮/舒巴坦、阿米卡星、美罗培南、亚胺培南等较为敏感,见表 2。

2.3 主要革兰阳性菌对抗菌药物的耐药性

霉素、替考拉宁、利福平等较为敏感,见表 3。

主要革兰阳性菌对青霉素、氨苄西林、哌拉西林 / 他唑巴坦、头孢菌素类、环丙沙星、左氧氟沙星等普遍耐药,但对万古

2.4 两组患者血清炎症因子与心肌酶谱指标水平比较

感染组患者 IL-6、Ang-2、TNF- $\alpha$ 、AST、LDH、CK 以及

表 2 主要革兰阴性菌对抗菌药物的耐药性(%)  
Table 2 Resistance of Gram-negative bacteria to antibacterial drugs(%)

Antibacterial drugs	<i>Klebsiella pneumoniae</i> (n=16)		<i>Escherichia coli</i> (n=9)		<i>Acinetobacter baumannii</i> (n=6)	
	n	Drug resistance rate	n	Drug resistance rate	n	Drug resistance rate
Penicillin	16	100.00	9	100.00	6	100.00
Piperacillin/sulbactam	0	0.00	1	11.11	1	16.67
Amoxicillin	1	6.25	8	88.89	5	83.33
Ciprofloxacin	14	87.50	8	88.89	6	100.00
Levofloxacin	15	93.75	7	77.78	5	83.33
Cephalexin	15	93.75	8	88.89	6	100.00
Cefuroxime	14	87.50	8	88.89	5	83.33
Ceftriaxone	13	81.25	9	100.00	5	83.33
Cefoperazone/sulbactam	1	6.25	1	11.11	1	16.67
Gentamicin	15	93.75	7	77.78	6	100.00
Amikacin	1	6.25	2	22.22	1	16.67
Meropenem	1	6.25	1	11.11	1	16.67
Imipenem	1	6.25	1	11.11	1	16.67

表 3 革兰阳性菌对抗菌药物的耐药性(%)  
Table 3 Resistance of Gram-positive bacteria to antimicrobial drugs(%)

Antibacterial drugs	<i>Streptococcus pneumoniae</i> (n=13)		<i>Staphylococcus aureus</i> (n=8)	
	Strains	Drug resistance rate	Strains	Drug resistance rate
Penicillin	11	84.62	8	100.00
Ampicillin	12	92.31	8	100.00
Piperacillin/tazobactam	7	53.85	8	100.00
Cephalexin	10	76.92	7	87.50
Cefuroxime sodium	10	76.92	6	75.00
Vancomycin	1	7.69	1	12.50
Teicoplanin	1	7.69	1	12.50
Rifamcin	1	7.69	1	12.50
Ciprofloxacin	11	84.62	7	87.50
Levofloxacin	8	61.54	6	75.00

表 4 两组患者血清炎症因子与心肌酶谱指标水平比较( $\bar{x}\pm s$ , U/L)  
Table 4 Comparison of serum inflammatory factors and myocardial enzymes in two groups( $\bar{x}\pm s$ , U/L)

Groups	IL-6	Ang-2	TNF- $\alpha$	AST	LDH	CK	CKMB
Infection group (n=67)	23.36 $\pm$ 2.84	154.54 $\pm$ 14.85	31.35 $\pm$ 6.23	61.96 $\pm$ 4.50	427.23 $\pm$ 48.92	269.84 $\pm$ 39.96	41.23 $\pm$ 8.78
Uninfected group (n=60)	13.35 $\pm$ 2.65	51.78 $\pm$ 8.52	12.44 $\pm$ 2.25	56.71 $\pm$ 5.35	396.12 $\pm$ 37.24	248.53 $\pm$ 42.95	35.77 $\pm$ 5.67
t	20.465	47.096	22.241	6.004	3.996	2.896	4.109
P	0.000	0.000	0.000	0.000	0.000	0.004	0.000

CKMB 水平均高于未感染组患者( $P<0.05$ ),见表 4。

## 2.5 感染组患者炎症因子与心肌酶谱指标相关性分析

经 Pearson 相关性分析可得,感染组患者血清 IL-6、Ang-2、

TNF- $\alpha$  水平与 AST、LDH、CK、CK-MB 水平均呈正相关( $P<0.05$ ),见表 5。

表 5 感染组患者炎症因子与心肌酶谱指标相关性分析

Table 5 Analysis of correlation between inflammatory factors and myocardial enzymes in patients with infection group

Index	AST		LDH		CK		CKMB	
	r	P	r	P	r	P	r	P
IL-6	0.389	0.001	0.392	0.000	0.403	0.000	0.311	0.000
Ang-2	0.405	0.000	0.312	0.000	0.326	0.000	0.431	0.000
TNF- $\alpha$	0.393	0.000	0.406	0.000	0.399	0.000	0.308	0.000

## 3 讨论

急性心肌梗死是心血管疾病中发病率较高的一种疾病,当急性心肌梗死发作时,可引发急性左心衰竭,心排血量降低,心肌缺血、缺氧造成心动功能减退,导致肺淤血、肺水肿以及免疫力下降,引发肺部感染,增大了治疗难度<sup>[12-14]</sup>。既往研究表明<sup>[15-17]</sup>,急性心肌梗死合并肺部感染患者在肺部感染得到控制后其心功能损伤往往也可随之缓解,但由于感染类型通常较为复杂,并且肺部感染患者亦存在多药耐药的病原菌,因此,及时判断急性心肌梗死合并肺部感染患者病情严重程度及对常用抗菌药物的耐药性进行研究对于临床治疗具有积极的意义。随着临床研究的深入,人们逐渐重视免疫因素在心血管疾病的发生发展中的作用,其水平变化可能对疾病的严重程度起到一定的提示效果<sup>[18-20]</sup>。

本次研究中 67 例感染组患者痰培养标本中共分离出病原菌 136 株,其中多药耐药菌 64 株,占比 47.06%,占比较高,这主要是由于我国抗菌药物不合理用药现象较为普遍,在患者未出现感染时就已存在多药耐药菌,同时也可能是因为急性心肌梗死合并肺部感染患者病情危急,感染复杂,引起多药耐药菌<sup>[21-23]</sup>。本研究革兰阳性菌占 40.63%(26/64),革兰阴性菌占 59.37%(38/64),提示多药耐药菌主要以革兰阴性菌为主。药敏研究发现革兰阴性菌对哌拉西林/舒巴坦、头孢哌酮/舒巴坦、阿米卡星、美罗培南、亚胺培南等较为敏感,而革兰阳性菌对万古霉素、替考拉宁、利福平等较为敏感,提示临床应根据药敏试验结果合理选用抗菌药物。同时本研究结果还表明,感染组患者血清炎症因子与心肌酶谱指标水平均高于未感染组患者,IL-6 作为前炎症细胞因子,具有减弱心肌收缩能力、产生局部斑块、促进急性期蛋白质合成等作用<sup>[24,25]</sup>,TNF- $\alpha$  具有多种生物活性,可损伤内皮细胞,促进粘附分子及其他炎症因子表达,参与动脉粥样硬化的各个阶段<sup>[26]</sup>,Ang-2 是促血管生成素家族中的一员,可破坏血管形成以及促进血管退化<sup>[27]</sup>。IL-6、Ang-2、TNF- $\alpha$  水平的升高均表明机体炎症反应加重。AST、LDH、CK 以及 CKMB 主要存在于心肌中,对急性心肌梗死具有较高的灵敏度,当发生急性心肌梗死后,器官及组织的缺血、缺氧现象在受到肺部感染,二次打击后,损伤加重,引发细胞坏死,AST、LDH、CK 以及 CKMB 等被释放入血<sup>[28-30]</sup>,致其心肌酶谱指标水平升高,IL-6、Ang-2、TNF- $\alpha$  则大量分泌,扩大炎症级联反应。

同时经 Pearson 相关性分析可得,感染组患者炎症因子与心肌酶谱指标水平均呈正相关,可见临床可参考上述指标用于判断患者病情严重程度。

综上所述,急性心肌梗死合并肺部感染患者多药耐药现象较为严重,临床应针对病原菌的耐药性合理选取抗菌药物,同时急性心肌梗死合并肺部感染患者炎症因子与心肌酶谱指标水平均较高,且相互之间存在一定的相关性,临床可参考上述指标用于判断患者病情严重程度。

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