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胫腓骨开放性骨折术后并发感染的病原菌分布、耐药性及影响因素分析 *

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摘要 目的：研究胫腓骨开放性骨折术后并发感染患者的病原菌分布、耐药性及影响因素。**方法：**回顾性分析 2014 年 1 月到 2018 年 1 月于华北石油管理局总医院接受治疗的 267 例单侧胫腓骨开放性骨折患者的临床资料，统计术后感染病例，分析胫腓骨开放性骨折术后感染患者的病原菌分布情况，分析主要革兰阳性菌和主要革兰阴性菌的耐药性，采用单因素和多因素 Logistic 回归分析术后患者发生感染的危险因素。**结果：**267 例患者发生术后感染 68 例，感染率为 25.47%；68 例患者共分离出病原菌 82 株，其中革兰阳性菌占 64.63%，革兰阴性菌占 28.05%，真菌占 7.32%；金黄色葡萄球菌、表皮葡萄球菌、粪肠球菌对青霉素、哌拉西林 / 他唑巴坦耐药性较高，对万古霉素、亚胺培南比较敏感；大肠埃希菌、阴沟肠杆菌、铜绿假单胞菌、鲍氏不动杆菌对头孢唑林耐药性较高，对亚胺培南和头孢哌酮 / 舒巴坦比较敏感；单因素分析显示：受伤原因、骨折部位、有无合并糖尿病、受伤至手术时间、清创情况、止血情况、引流情况、术后有无使用抗菌药物均是导致胫腓骨开放性骨折术后发生感染的相关因素（P<0.05）；多因素 Logistic 回归分析显示：受伤至手术时间 >6 h、清创不彻底、止血不彻底、引流不通畅、术后未使用抗菌药物均是导致胫腓骨开放性骨折术后发生感染的危险因素（P<0.05）。**结论：**胫腓骨开放性骨折患者术后感染以革兰阳性菌为主，其对青霉素、哌拉西林 / 他唑巴坦敏感性较低，临床上应针对危险因素采取有效预防措施，并根据药敏试验选择有效药物治疗。

关键词：胫腓骨开放性骨折；术后感染；病原菌；耐药性；影响因素

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Analysis of Distribution, Drug Resistance and Influencing Factors of Pathogen Causing Postoperative Infection in Open Tibial and Fibular Fractures*

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ABSTRACT Objective: To study the distribution,drug resistance and influencing factors of pathogen causing postoperative infection in open tibial and fibular fractures. **Methods:** The clinical data of 267 patients with open fracture of tibia and fibula who were treated in General Hospital of North China Petroleum Administration from January 2014 to January 2018 were retrospectively analyzed. Postoperative infection cases was counted, the distribution of pathogens causing postoperative infection in open tibial and fibular fracture was analyzed, and antimicrobial resistance of major gram-positive bacteria and major gram negative bacteria was analyzed. Univariate and multivariate Logistic regression analysis was used to analyze the risk factors of postoperative infection. **Results:** Among 267 patients, 68 cases had occurred postoperative infection, the infection rate was 25.47%. 82 strains of pathogen were isolated from 68 patients, of which gram positive bacteria was accounted for 64.63%, gram-negative bacteria was accounted for 28.05%, fungi was accounted for 7.32%. *Staphylococcus aureus*, *staphylococcus epidermidis*, and *enterococcus faecalis* were more resistant to penicillin, piperacillin/tazobactam, which were more sensitive to vancomycin and imipenem. *Escherichia coli*, *enterobacter cloacae*, *pseudomonas aeruginosa* and *acinetobacter baumannii* were more resistant to cefazolin, which were more sensitive to imipenem and cefoperazone/sulbactam. Univariate analysis showed that the causes of injury, fracture site, diabetes, injury to operation time, debridement, hemostasis, drainage, and no use of antibiotics were all related factors causing postoperative infection in open tibial and fibular fractures (P<0.05). Multivariate Logistic regression analysis showed that the injury to the operation time >6 h, incomplete debridement, incomplete hemostasis, obstructed drainage and postoperative no use of antibiotics were all risk factors causing postoperative infection in open tibial and fibular fractures(P<0.05). **Conclusion:** Postoperative infection of tibiofibula open fractures is mainly caused by Gram-positive bacteria, and their sensitivity to penicillin and piperacillin/tazobactam is lower. Clinically, effective preventive measures should be taken against risk factors, and effective drug therapy should be selected according to drug sensitivity test.

Key words: Open fracture of the tibia and fibula; Postoperative infection; Pathogen; Drug resistance; Influence factor

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前言

胫腓骨骨折是临床上常见的骨折类型之一，其中胫骨骨折占所有开放性骨折的 23.5%，而其中 50%的骨折是由交通事故和直接暴力所导致[1-3]。由于胫腓骨的解剖结构特殊，骨折易伴有软组织挫裂、撕脱，甚至引起深层肌腱、神经、血管的损伤，合并有创面感染，治疗起来比较复杂[4-6]。目前治疗方法较多，包括外固定支架、钢板内固定、闭合髓内钉等，虽然临床效果良好，但是术后感染率较高，严重影响患者术后康复[7,8]。因此，寻找有效的方式预防术后感染并控制术后感染发生的危险因素具有重要的临床意义，而分析病原菌的分布和耐药情况有利于指导临床用药[9,10]。本研究通过观察胫腓骨开放性骨折术后感染患者的病原菌分布和耐药性情况，以及对发生感染的相关危险因素进行分析，旨在为预防和控制术后感染及临床用药提供数据支持。

1 资料和方法

1.1 一般资料

对 2014 年 1 月到 2018 年 1 月期间入住华北石油管理局总医院并接受治疗的 267 例单侧胫腓骨开放性骨折患者的临床资料进行回顾性分析，纳入标准：① 患者年龄 18 岁以上，80 岁以下；② 经 X 线或 CT 影像学检查确诊为单侧胫腓骨开放性骨折；③ 患者病历资料、影像资料、随访资料均保存完整。排除标准：① 既往有胫腓骨创伤手术史或病理性骨折；② 双侧胫腓骨开放性骨折；③ 合并其他部位的骨折；④ 合并有出、凝血功能障碍患者；⑤ 合并有严重心肺疾病不能耐受手术者；⑥ 术后失访病例。

1.2 术后感染判断标准

根据《医院感染诊断标准》[11]确诊感染：① 症状表现为骨折感染部位出现红肿热痛、渗液或有脓液存在；② 白细胞、降钙素原测定、血培养、细菌培养等检查结果均符合感染标准。

1.3 治疗方法

所有患者入院后均给予相关对症治疗，进行相关检查，请相关科室会诊，排除手术风险，各项指标平稳后进行清创探查，根据 Gustilo-Anderson[12]分型对 Ⅰ 型行 Ⅰ 期内固定术治疗，彻底清除污染物和坏死组织，沿着肌腱、神经、血管进行探查，复位后根据患者骨折特点选取适当钢板螺钉内固定治疗。Ⅱ、Ⅲ 型骨折患者则根据污染和骨折程度及患者病情进行分期治疗，清创后根据骨折移位、成角、旋转等实际情况，积极止血，选择外固定支架治疗，按照软组织损伤程度，选择皮瓣移植或 VSD 负压引流。术后尽早指导患者功能锻炼，预防血栓和感染。

1.4 病原菌的采集、鉴定及药敏实验方法

病原菌的采集：按照无菌原则，采集骨折部位的分泌物或者引流物标本，进行细菌分离培养，来自于不同部位的相同菌株则视为同一菌株。病原菌鉴定方法[13]：根据革兰氏染色结果，进行触酶和氧化酶实验，鉴定系统中的 ID 百分比超过 99%，鉴定病原菌的类型。药敏实验方法：采用法国生物－梅里埃（BIOMERIEUX）公司生产的 VITEK-2 型全自动微生物分析仪进行药敏性的检测。

1.5 资料收集

采集单侧胫腓骨开放性骨折患者的一般资料，包括性别、骨折部位、受伤原因、合并糖尿病、受伤至手术时间、清创情况、止血情况、引流情况、术后使用抗菌药物等。

1.6 统计学方法

采用 SPSS25.0 统计学软件，计量资料用（$\bar{x}\pm s$）表示，采用 t 检验；计数资料以%表示，采用 x^2 检验；采用单因素和多因素 Logistic 回归分析胫腓骨开放性骨折术后发生感染的危险因素，以 $P<0.05$ 为差异有统计学意义。

2 结果

2.1 胫腓骨开放性骨折术后并发感染患者病原菌分布情况

267 例患者发生术后感染 68 例，感染率为 25.47%；68 例患者共分离出病原菌 82 株，其中混合感染 27 例占 32.93%，单一感染 55 例占 67.07%，病原菌中革兰阳性菌 53 株占 64.63%，革兰阴性菌 23 株占 28.05%，真菌 6 株占 7.32%，见表 1。

表 1 胫腓骨开放性骨折术后并发感染患者病原菌分布情况

Table 1 Distribution of pathogens causing postoperative infection in open fracture of tibia and fibula

Pathogenic bacteria		n	Constituent ratio（%）
Gram-positive bacteria（n=53）	*Staphylococcus aureus*	24	29.27
	Staphylococcus epidermidis	13	15.85
	Enterococcus faecalis	8	9.76
	Streptococcus pyogenes	5	6.10
	Staphylococcus haemolysin	3	3.66
Gram-negative bacteria（n=23）	*Escherichia coli*	11	13.41
	Enterobacter cloacae	5	6.10
	Pseudomonas aeruginosa	3	3.66
	Acinetobacter baumannii	2	2.44
	Enterobacter Enterobacter	2	2.44
Fungus		6	7.32
Total		82	100.00

2.2 胫腓骨开放性骨折术后并发感染患者主要革兰阳性菌耐药性分析

金黄色葡萄球菌对青霉素、哌拉西林/他唑巴坦、头孢曲松耐药性较高，对万古霉素、亚胺培南、左氧氟沙星比较敏感，表皮葡萄球菌对青霉素、哌拉西林/他唑巴坦耐药性较高，对万古霉素、亚胺培南、左氧氟沙星、环丙沙星比较敏感，粪肠球菌对青霉素、哌拉西林/他唑巴坦耐药性较高，对万古霉素、亚胺培南比较敏感，见表2。

表2 胫腓骨开放性骨折术后并发感染患者主要革兰阳性菌耐药性分析

Table 2 Drug resistance analysis of main gram-positive bacteria causing postoperative infection in open fracture of tibia and fibula

Antiseptic drugs	Gram-positive bacteria					
	Staphylococcus aureus(n=24)		*Staphylococcus epidermidis*(n=13)		*Enterococcus faecalis*(n=8)	
	n	Drug resistance rate(%)	n	Drug resistance rate(%)	n	Drug resistance rate(%)
Penicillin	23	95.83	10	76.92	5	62.50
Cefatriaxone	12	50.00	5	38.46	3	37.50
Cefazolin	9	37.50	6	46.15	2	25.00
Gentamicin	6	25.00	5	38.46	2	25.00
Clindamycin	4	16.67	3	23.08	1	12.50
Ciprofloxacin	2	8.33	1	7.69	2	25.00
Levofloxacin	1	4.17	1	7.69	2	25.00
Piperacillin/tazobactam	18	75.00	10	76.92	5	62.50
Imipenem	1	4.17	0	0.00	0	0.00
Vancomycin	0	0.00	0	0.00	0	0.00

2.3 胫腓骨开放性骨折术后并发感染患者主要革兰阴性菌耐药性分析

大肠埃希菌对头孢唑林和克林霉素耐药性较高，对亚胺培南和头孢哌酮/舒巴坦比较敏感，阴沟肠杆菌对头孢唑林和阿莫西林耐药性较高，对亚胺培南和左氧氟沙星敏感，铜绿假单胞菌对头孢唑林和氯霉素耐药，对亚胺培南和头孢哌酮/舒巴坦敏感，鲍氏不动杆菌对氯霉素和阿莫西林耐药，对头孢唑林耐药性也较高，对亚胺培南和头孢哌酮/舒巴坦敏感，见表3。

表3 胫腓骨开放性骨折术后并发感染患者主要革兰阴性菌耐药性分析

Table 3 Drug resistance analysis of main gram-nagative bacteria causing postoperative infection in open fracture of tibia and fibula

Antiseptic drugs	Gram-negative bacteria							
	Escherichia coli(n=11)		*Enterobacter cloacae*(n=5)		*Pseudomonas aeruginosa* (n=3)		*Acinetobacter baumannii* (n=2)	
	n	Drug resistance rate(%)	n	Drug resistance rate(%)	n	Drug resistance rate(%)	n	Drug resistance rate(%)
Clindamycin	8	72.73	3	60.00	1	33.33	1	50.00
Cefotaxime	6	54.55	2	40.00	1	33.33	1	50.00
Amoxicillin	6	54.55	4	80.00	2	66.67	2	100.00
Ceftazidime	7	63.64	2	40.00	2	66.67	1	50.00
Norfloxacin	5	45.45	3	60.00	2	66.67	1	50.00
Chloramphenicol	4	36.36	2	40.00	3	100.00	2	100.00
Levofloxacin	5	45.45	0	0.00	1	33.33	1	50.00
Cefoperazone/sulbactam	1	9.09	1	20.00	0	0.00	0	0.00
Imipenem	0	0.00	0	0.00	0	0.00	0	0.00
Cefazolin	10	90.91	5	100.00	3	100.00	1	50.00

2.4 胫腓骨开放性骨折术后发生感染相关因素的单因素分析

患者的受伤原因、骨折部位、有无合并糖尿病、受伤至手术时间、清创情况、止血情况、引流情况、术后有无使用抗菌药物均是导致胫腓骨开放性骨折术后发生感染的相关因素（$P<0.05$），而性别与胫腓骨开放性骨折术后发生感染无关（$P>0.05$），见表4。

2.5 胫腓骨开放性骨折术后感染危险因素的多因素 Logistic 回归分析

以术后是否发生感染为因变量，以上述单因素分析中比较有统计学意义的指标为自变量纳入多因素 Logistic 回归分析

模型，结果显示：受伤至手术时间 >6h、清创不彻底、止血不彻底、引流不通畅、术后未使用抗菌药物均是导致胫腓骨开放性骨折术后发生感染的危险因素（P<0.05），见表 5。

表 4 胫腓骨开放性骨折术后发生感染相关因素的单因素分析

Table 4 Univariate analysis of related factors causing postoperative infection in open fracture of tibia and fibula

Factors		Total（n=267）	Cases of infection（n=68）	Infection rate（%）	x^2	P
Gender	Male	190	47	24.74	0.186	0.667
	Female	77	21	27.27		
Cause of injury	Traffic accident injury	121	42	34.71	65.307	0.000
	Falling injury at high altitude	72	13	18.06		
	Direct violence	44	9	20.45		
	Motor injury	30	4	13.33		
Fracture site	Near end	43	9	20.93	75.490	0.000
	Middle part	103	27	26.21		
	Distal end	121	32	26.45		
Diabetes mellitus	Yes	143	47	32.87	8.880	0.003
	No	124	21	16.94		
Injury to operation time（h）	≤ 6	139	23	16.55	12.157	0.000
	>6	128	45	35.16		
Debridement	Thorough	105	15	14.29	11.400	0.000
	Not thorough	162	53	32.72		
Hemostasis	Thorough	113	18	15.93	9.391	0.002
	Not thorough	154	50	32.47		
Drainage situation	Unobstructed	142	23	16.20	13.734	0.000
	Not unobstructed	125	45	36.00		
Postoperative use of antimicrobial agents	Yes	119	19	15.97	10.211	0.001
	No	148	49	33.11		

表 5 胫腓骨开放性骨折术后感染危险因素的多因素 Logistic 回归分析

Table 5 Multivariate Logistic regression analysis of risk factors causing postoperative infection in open fracture of tibia and fibula

Variable	β	Wald x^2	P	OR	95% CI
Injury to operation time>6 h	0.211	4.792	0.029	1.235	1.022～1.493
Debridement is not thorough	1.439	10.143	0.001	0.237	0.098～0.575
Hemostasis is not thorough	1.868	19.669	0.000	0.154	0.068～0.353
Drainage is not unobstructed	3.429	36.739	0.000	0.032	0.011～0.098
No antibiotics were used after operation	4.875	21.317	0.000	0.008	0.001～0.060

3 讨论

胫腓骨属于人体长管状骨中承重骨骼，骨性解剖结构特殊，胫骨干中下三分之一交界处为其解剖薄弱处[14-16]。胫腓上下关节为微动关节，胫骨位于前内侧皮下的骨突部位，均易导致开放性骨折，同时腓总神经走形表浅，胫后动脉位置固定，受伤后易形成筋膜间室综合征[17,18]。目前针对胫腓骨开放性骨折治疗方法众多，包括外固定支架、髓内钉、钢板螺钉内固定等，钢板内固定容易形成应力遮挡，髓内钉易造成骨折畸形愈合，而外固定支架虽然对软组织创伤和骨端血运破坏小，但是可能引起固定针松动和切割、针道感染等问题[19,20]。手术对软组织、骨膜和血运的破坏，加之细菌入侵繁殖后造成的感染，成为胫腓骨开放性骨折术后严重并发症[21]。尽管随着医疗技术的发展，骨科术后感染发生率逐年降低，但是术后一旦发生感染，给患者和家庭带来严重的负担，影响患者生活质量[22]。

本研究中，267 例患者发生术后感染 68 例，感染率为 25.47%，这比常见骨折术后的感染率明显增高，可能与骨折部位、纳入病例的选择、手术方法等相关。68 例患者共分离出病原菌 82 株，病原菌中革兰阳性菌 53 株占 64.63%，革兰阴性菌 23 株占 28.05%，真菌 6 株占 7.32%，这与 Rodriguez L[23]报道的结果相一致，胫腓骨开放性骨折术后感染患者的病原菌以革兰阳性菌为主。本研究结果显示，革兰阳性感染病原菌中以金黄色葡萄球菌、表皮葡萄球菌和粪肠球菌为主占 84.91%，通过药敏实验结果提示三者均对青霉素、哌拉西林 / 他唑巴坦耐药性

较高,对万古霉素、亚胺培南比较敏感。这与赵新刚等[24]研究结果相似。由于病原菌耐药性相似,可能与患者住院期间院内感染有一定的关系,因此在平时应注意病床和病房的消毒,感染病人的隔离,以阻断感染机会。本研究结果显示,革兰阴性感染病原菌中以阴沟肠杆菌、大肠埃希菌、铜绿假单胞菌以及鲍氏不动杆菌为主,以上均对头孢唑林敏感性较低,对亚胺培南和头孢哌酮/舒巴坦比较敏感,此外大肠埃希菌对克林霉素敏感性较低,鲍氏不动杆菌对氯霉素和阿莫西林耐药,铜绿假单胞菌对氯霉素耐药,阴沟肠杆菌对阿莫西林敏感性较低,而对左氧氟沙星敏感。因此,结合药敏实验在发生比较严重的感染时可采用碳青霉烯类抗菌药物治疗,但是由于易产生二重感染,所以根据药敏结果合理选择用药,密切观察病情非常重要[25,26]。

本研究多因素 Logistic 回归分析结果显示,受伤至手术时间 >6h、清创不彻底、止血不彻底、引流不通畅、术后未使用抗菌药物是导致胫腓骨开放性骨折术后发生感染的危险因素($P<0.05$)。分析如下:① 受伤至手术时间 >6 h:胫腓骨开放性骨折 6 h 内为新鲜伤口,属于清创黄金时间,若创口暴露在空气中时间过长,细菌更容易入侵繁殖,可能部分患者 6 h 内未能及时到达医院接受创口清洁和手术治疗,导致术后感染;② 清创不彻底:开放性创面污染有异物、坏死和失活组织,容易滋生细菌,需要彻底清创才能为后期组织修复提供良好环境;③ 止血不彻底:开放性骨折后动静脉损伤,血液为细菌繁殖提供条件,止血不彻底可能导致部分毛细血管仍有出血,从而积血引起感染[27,28];④ 引流不通畅:负压充分引流,消除积液积血,可以减轻血肿,而引流管堵塞,未能及时彻底引流出积液积血可能导致感染发生;⑤ 术后未使用抗菌药物:临床研究证实术后使用抗菌药物可有效降低术后感染率,Gustilo-Anderson Ⅰ型和Ⅱ型部分患者术后未使用抗菌药物,可能导致术后发生感染[29,30]。

综上所述,胫腓骨开放性骨折患者术后以革兰阳性菌感染为主,其对青霉素、哌拉西林/他唑巴坦敏感性较低,临床上应针对危险因素采取有效预防措施,并根据药敏试验选择有效药物治疗。由于本研究为回顾性研究,病例选择可能存在一定的偏倚,纳入病例数较少,可能结果有误差,有待大样本多中心的进一步研究。

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