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·2019冠状病毒病·

感染奥密克戎变异株的2019冠状病毒病轻型和普通型患者核酸检测转阴时间影响因素分析

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[摘　要]　**目的**:观察感染奥密克戎变异株的2019冠状病毒病(COVID-19)轻型和普通型患者临床特征,分析影响患者病毒核酸检测转阴时间的相关因素。**方法**:回顾性分析2022年4月12日至5月26日上海某方舱医院收治的1781例COVID-19患者的临床资料,包括患者年龄、性别、身高、体重、临床症状、基础疾病史、COVID-19疫苗接种情况、治疗用药情况及核酸检测转阴时间等。采用单因素分析和多因素logistic回归分析患者核酸检测转阴时间的影响因素。**结果**:1781例患者中,男性995例,女性786例,年龄中位数为39(30,52)岁,超重偏肥胖[体质指数(BMI)为24 kg/cm^{2}以上]727例(40.8%),存在基础疾病413例(23.2%);未接种COVID-19疫苗205例(11.5%),接种疫苗1576例(88.5%);有1种及以上症状1233例(69.2%),以咳嗽(60.3%)、咳痰(50.4%)、发热(36.9%)多见;接受中药治疗1444例(81.0%),西药治疗78例(4.4%),中西医结合治疗14例(0.8%),未接受药物治疗245例(13.8%),所有患者经过对症处理后均改善,全部痊愈出院,核酸检测转阴中位时间为10.3(7.4,12.4)d。单因素和多因素分析结果显示,年龄为60岁及以上(OR=1.537,95%CI: 1.116~2.115,P<0.01)、BMI为24 kg/cm^{2}以上(OR=1.344,95%CI: 1.106~1.634,P<0.01)、合并高血压(OR=1.518,95%CI: 1.094~2.106,P<0.05)是患者核酸检测转阴时间延长的独立危险因素;接种COVID-19疫苗(OR=0.548,95%CI: 0.398~0.755,P<0.01)是保护因素,即接种COVID-19疫苗核酸检测转阴时间缩短。**结论**:奥密克戎变异株感染的COVID-19患者临床症状相对较轻,病情隐匿,患者年龄为60岁及以上、未接种COVID-19疫苗、BMI为24 kg/cm^{2}以上、合并高血压是核酸检测转阴时间延长的独立影响因素。

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[关键词] 奥密克戎变异株;2019冠状病毒病;临床表现;核酸检测;影响因素
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Influencing factors of nucleic acid negative conversion in patients with mild and common COVID-19 induced by the Omicron variant of SARS-COV-2

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[**Abstract**] **Objective**: To observe the clinical characteristics of mild and common COVID-19 patients infected with the Omicron variant, and to analyze related factors affecting the time to negative conversion of viral nucleic acid detection. **Methods**: Clinical data of 1781 patients with coronavirus disease 2019 (COVID-19) admitted to a cabin hospital in Shanghai from April 12 to May 26, 2022, were retrospectively analyzed, including age, gender, height, weight, clinical symptoms, comorbid diseases, COVID-19 vaccination, treatment, and nucleic acid negative conversion time. Univariate and multivariate logistic regression analyses were used to analyze the influencing factors of nucleic acid negative conversion time. **Results**: Among the 1781 patients, 995 were male and 786 were female, with a median age of 39 (30, 52) years. There were 727 patients (40.8%) with overweight and obesity [body mass index (BMI) > 24 kg/cm^2) and 413 patients (23.2%) had comorbid diseases. 205 cases (11.5%) were not vaccinated while 1576 cases were vaccinated. There were 1233 cases (69.2%) with one or more symptoms. The main clinical symptoms were cough (60.3%), expectoration (50.4%) and fever (36.9%). 1444 cases (81.0%) were treated with Chinese medicine, 78 cases (4.4%) were treated with western medicine, 14 cases (0.8%) were treated with integrated Chinese and western medicine, and 245 cases (13.8%) did not receive any medical treatment. All patients improved and were discharged. The median nucleic acid negative conversion time was 10.3 (7.4, 12.4) d. Univariate and multivariate analysis showed that, age ≥ 60 years (OR=1.537, 95%CI: 1.116–2.115, P<0.01), BMI > 24 kg/cm^2 (OR=1.344, 95%CI: 1.106–1.634, P<0.01) and hypertension (OR=1.518, 95%CI: 1.094–2.106, P<0.05) were independent risk factors for prolonged nucleic acid negative conversion. COVID-19 vaccination (OR=0.548, 95%CI: 0.398–0.755, P<0.01) was a protective factor, that is, vaccination shortened the time for the nucleic acid test to become negative. **Conclusions**: The symptoms of the Omicron variant infection were relatively mild and occult. Age ≥ 60 years old, comorbid hypertension, no vaccination and BMI > 24 kg/cm^2 are

independent influencing factors for prolonged nucleic acid negative conversion.

[**Key words**] Omicron variant; Corona virus disease 2019; Clinical manifestation; Nucleic acid testing; Influential factors

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[**缩略语**] 2019冠状病毒病(coronavirus disease 2019,COVID-19);严重急性呼吸综合征冠状病毒2(severe acute respiratory syndrome coronavirus 2,SARS-CoV-2);体质指数(body mass index,BMI);比值比(odds ratio,OR);置信区间(confidence interval,CI)

从COVID-19疫情开始至今,疫情的广泛传播与SARS-CoV-2不断进化及变异密切相关,后者给全世界包括我国在内的防疫工作带来巨大挑战。2021年12月9日,我国首次在天津入境闭环管理人员中检出SARS-CoV-2奥密克戎变异株[1]。有文献报道,奥密克戎变异株与SARS-CoV-2野生株或其他变异株相比,具有所致疾病潜伏期短、代际间隔小、病毒传播快、无症状感染者比例高以及病死率低等特点[2]。COVID-19分为轻型、普通型、重型和危重型,奥密克戎变异株感染患者轻型和普通型占80%以上[3-4]。病毒核酸检测结果阳性是确诊COVID-19的依据。核酸检测结果从阳性转为阴性表明患者体内病毒不再复制,机体恢复正常。尽管奥密克戎变异株毒力减弱,但传播力增强。感染患者携带病毒时间越长越不利于疫情控制。因此,缩短感染患者核酸检测阳性时间,促进其尽快转阴对疫情防控具有重要意义。本研究对2022年上海地区新一轮COVID-19疫情中的轻型和普通型病例的临床特征及核酸检测转阴时间进行分析,为现阶段疫情防控和临床诊治提供依据。

1 对象与方法

1.1 对 象

收集2022年4月12日至5月26日上海某方舱医院收治的经基因测序诊断的奥密克戎变异株感染COVID-19患者。纳入标准:①根据《新型冠状病毒肺炎诊疗方案(试行第九版)》[3]诊断标准及临床分型确定为轻型、普通型COVID-19者;②年龄为18岁及以上者;③年龄、性别、身高、体重、临床症状、基础疾病史、COVID-19疫苗接种情况及核酸检测转阴时间等资料较完整者。研究方案通过中国人民解放军联勤保障部队第九〇八医院伦理委员会审查(908yyLL093),豁免患者及法定监护人/近亲属书面知情同意。

1.2 治疗方案、出院标准及相关定义

所有患者的治疗方案及出院标准严格按照《新型冠状病毒肺炎诊疗方案(试行第九版)》[3]执行。核酸检测转阴时间指患者第二次核酸检测阴性时间(连续两次呼吸道标本核酸检测阴性,采样时间至少间隔24 h)与第一次核酸检测阳性的日期之差。

1.3 统计学方法

采用SPSS 26.0软件进行统计分析。服从正态分布的计量资料采用均数±标准差($\bar{x}\pm s$)表示,不服从正态分布的计量资料采用中位数(上下四分位数)[$M(Q_1, Q_3)$]表示,计数资料采用例数(百分比)[n(%)]表示。核酸检测转阴时间影响因素的单因素分析采用Mann-Whitney U检验或Kruskal-Wallis H检验,多因素分析采用多因素logistic线性回归分析,$P<0.05$为差异有统计学意义。

2 结 果

2.1 1781例纳入患者基本情况

纳入研究的1781例患者中,男性995例,女性786例,年龄中位数为39(30,52)岁。BMI在正常范围(18~24 kg/cm^2)1008例(56.6%),BMI为18 kg/cm^{2}以下46例(2.6%),BMI为24 kg/cm^{2}以上727例(40.8%)。413例(23.2%)患者存在基础疾病,其中高血压217例,糖尿病80例,脑梗死20例,心肌梗死18例,慢性胃肠道疾病163例,慢性肾病22例,肿瘤17例。未接种COVID-19疫苗205例(11.5%),接种疫苗1576例(88.5%)。有一种及以上症状者1233例(69.2%),其中以咳嗽(60.3%)、咳痰(50.4%)、发热(36.9%)多见。接受中药治疗

1444例(81.0%),西药治疗78例(4.4%),中西医结合治疗14例(0.8%),未用药245例(13.8%),所有患者经过对症处理后症状均改善,全部痊愈出院,核酸检测转阴中位时间为10.3(7.4, 12.4) d。

2.2　1781例患者核酸检测转阴时间影响因素的单因素分析结果

单因素分析结果显示,年龄为60岁及以上、未接种COVID-19疫苗、BMI为24 kg/cm^{2}以上,以及合并高血压、糖尿病、脑梗死、心肌梗死、慢性胃肠道疾病、慢性肾病、肿瘤患者的核酸检测转阴时间较长(均P<0.05),见表1。结果提示,核酸检测转阴时间可能与患者年龄、BMI、合并基础疾病和COVID-19疫苗接种情况相关。

2.3　1781例患者核酸检测转阴时间影响因素的多因素logistic回归分析结果

将所有患者按照核酸检测转阴中位时间进行分组,将单因素分析中有统计学意义的因素作为自变量纳入回归方程,以核酸检测转阴时间是否为10 d及以上为因变量,采用逐步后退法进行logistic回归分析。结果显示,年龄为60岁及以上(OR=1.537, 95%CI: 1.116~2.115, P<0.01)、BMI为24 kg/cm^{2}以上(OR=1.344, 95%CI: 1.106~1.634, P<0.01)、合并高血压(OR=1.518, 95%CI: 1.094~2.106, P<0.05)是患者核酸检测转阴时间延长的独立危险因素,接种COVID-19疫苗(OR=0.548, 95%CI: 0.398~0.755, P<0.01)是保护因素,见表2。

表 1　1781例COVID-19患者核酸检测转阴时间影响因素的单因素分析结果

Table 1　Results of univariate analysis on influencing factors of nucleic acid negative conversion time in COVID-19 patients

[M (Q_1, Q_3)]

因素		n	核酸检测转阴时间(d)	P 值
性别	男	995	10.3 (7.4, 12.4)	>0.05
	女	786	9.4 (7.4, 12.4)	
年龄	60岁以下	1558	9.4 (7.4, 12.4)	<0.01
	60岁及以上	223	11.4 (9.4, 11.4)	
就诊时有无症状	有	1233	10.3 (7.4, 12.4)	>0.05
	无	548	9.4 (7.4, 12.4)	
COVID-19疫苗接种	是	1576	9.4 (7.4, 12.4)	<0.01
	否	205	11.4 (8.4, 14.4)	
治疗	中药	1444	10.4 (7.4, 12.4)	>0.05
	西药	78	10.3 (7.4, 12.4)	
	中西医结合	14	10.4 (7.4, 16.3)	
	未用药	245	9.4 (6.4, 12.4)	
BMI(kg/cm^2)	<18	46	8.4 (6.4, 11.1)	<0.01
	18~24	1008	9.4 (7.4, 12.3)	
	>24	727	10.3 (7.4, 13.3)	
合并高血压	有	217	11.4 (9.4, 13.4)	<0.01
	无	1564	9.4 (7.4, 12.4)	
合并糖尿病	有	80	10.4 (8.4, 13.4)	<0.05
	无	1701	9.5 (7.4, 12.4)	
合并脑梗死	有	20	12.3 (10.6, 13.9)	<0.05
	无	1761	10.3 (7.4, 12.4)	
合并心肌梗死	有	18	13.3 (10.4, 17.4)	<0.01
	无	1763	10.3 (7.4, 12.4)	
合并慢性胃肠道疾病	有	163	10.4 (8.3, 13.4)	<0.05
	无	1618	9.4 (7.4, 12.4)	
合并慢性肾病	有	22	11.8 (9.9, 14.9)	<0.05
	无	1759	10.3 (7.4, 12.4)	
合并肿瘤	有	17	12.4 (8.9, 15.8)	<0.05
	无	1764	10.3 (7.4, 12.4)	

COVID-19:2019冠状病毒病;BMI:体质指数.

3　讨　论

COVID-19疫情是我国乃至全球遭遇的传播速度快、感染范围广、防控难度大的公共卫生事件。本文回顾性分析2022年3月开始在上海爆发的奥密克戎变异株感染1781例COVID-19患者的临床资料发现,60岁以下患者占比87.5%,感染主体逐渐趋于年轻化,这也可能与年轻人出行或社交活动较老年人多,感染的概率增大有关。在临床症状方面,无症状感染者占30.8%,有一种及以上症状的感染者占69.2%,主要以咳嗽、咳痰为主,发热次之,与疫情初期病例的临床症状(发热占75%以上)[5-6]有所不同。证明病毒随着不断传播和演变,毒力较前减弱,但咳嗽、咳痰、发热仍是COVID-19患者的主要临床症状,与英国[7]、智利[8]、美国[9]等相继报道的奥密克戎变异株感染者临床表现多为轻症、上呼吸道症状为主、住院率和病死率较前降低一致。本文资料中患者疫苗接种率为88.5%,与张洪玲等[10]报道相近,表明全国普及疫苗接种取得成效,另一方面提示奥密克戎变异株可逃过初次感染引发的免疫防线[11],因此继续研发疫苗,提高疫苗的有效性对于今后疫情

表 2 1781例COVID-19患者核酸检测转阴时间影响因素的多因素logistic回归分析结果

Table 2 Results of multivariate logistic regression analysis on influencing factors of nucleic acid negative conversion time in patients with COVID-19

因 素	回归系数	标准误差	Wald χ^2值	*P* 值	*OR* 值	95%*CI*
年龄为60岁及以上	0.430	0.163	6.944	<0.01	1.537	1.116~2.115
接种COVID-19疫苗	–0.601	0.163	13.536	<0.01	0.548	0.398~0.755
BMI为24 kg/cm^{2}以上	0.296	0.100	8.845	<0.01	1.344	1.106~1.634
合并高血压	0.417	0.167	6.233	<0.05	1.518	1.094~2.106
合并糖尿病	–0.128	0.256	0.249	>0.05	0.880	0.533~1.453
合并脑梗死	0.618	0.593	1.088	>0.05	1.856	0.581~5.930
合并心肌梗死	1.508	0.776	3.773	>0.05	4.519	0.986~20.699
合并慢性胃肠道疾病	0.210	0.171	1.514	>0.05	1.234	0.883~1.724
合并慢性肾病	0.743	0.536	1.918	>0.05	2.102	0.735~6.016
合并肿瘤	0.205	0.540	0.144	>0.05	1.228	0.426~3.541

COVID-19:2019冠状病毒病;BMI:体质指数.

的防控十分重要。

SARS-CoV-2核酸检测是COVID-19诊断的重要证据[12-13],连续两次呼吸道标本核酸检测阴性是患者治愈和解除隔离的主要参考指标。董玉颖等[14]研究显示,COVID-19疫情初期感染者从暴露时间计算得平均核酸检测转阴时间为(24.08 ± 1.17)d;龚惠莉等[15]对刚爆发时武汉市金银潭医院收治的179例COVID-19患者进行回顾性分析得出平均核酸检测转阴时间为(19.3 ± 4.2) d 。本文资料显示,1781例患者核酸检测转阴中位时间为10.3 d,较COVID-19疫情爆发初期病例的核酸检测转阴时间明显缩短,其可能与病毒本身的变异、逐渐成熟的治疗方案以及COVID-19疫苗的广泛接种有关。

本文资料显示,年龄为60岁及以上、BMI为24 kg/cm^{2}以上、合并高血压是患者核酸检测转阴时间延长的危险因素,而接种COVID-19疫苗是保护因素。张泽娜等[16]通过追踪230例COVID-19患者的1568名密切接触者发现,61岁及以上的密切接触者核酸检测阳性率为12%,明显高于其他年龄段密切接触者。老年人阳性率高、核酸检测转阴时间延长可能与其自身免疫屏障较差、易被病毒突破相关,因此建立自身免疫屏障十分重要。疫苗接种是建立免疫屏障的重要手段。本文资料显示,是否接种COVID-19疫苗是患者核酸检测转阴时间的独立影响因素,未接种疫苗者核酸检测转阴时间明显延长,提示接种COVID-19疫苗能够起到保护作用,与国外研究报道的接种COVID-19疫苗具有一定的保护作用,特别是接种了加强针保护作用明显[17-19]结果一致,因此普及COVID-19疫苗接种对于现阶段COVID-19疫情防控仍然重要,尤其是要提高老年人的疫苗接种率。肥胖是患者核酸检测转阴时间的独立影响因素。一项家庭传播研究结果显示,肥胖成年人比非肥胖成年人携带甲型流感病毒的时间长[20]。推测肥胖的COVID-19患者病毒释放时间更长,提示临床上应重视肥胖COVID-19患者的管理。本文资料还显示,合并基础疾病特别是高血压是患者核酸检测转阴时间延长的独立危险因素,与相关研究报道的结果一致[21-24],分析原因可能与肾素–血管紧张素系统有关。SARS-CoV-2的受体血管紧张素转换酶2是肾素–血管紧张素系统的重要组成部分,合并高血压的患者使用血管紧张素转化酶抑制剂/血管紧张素Ⅱ受体阻滞药药物可能使血管紧张素转换酶2表达上调,增加了SARS-CoV-2的感染风险,从而导致病情加重、病毒清除时间延长[25-28]。本文资料显示,核酸检测转阴时间不受性别的影响,与文献[23-24]提示男性是奥密克戎变异株感染后不良预后的危险因素不同,可能与本研究纳入的均是轻型、普通型患者有关。

综上所述,本文资料提示,年龄为60岁及以上、未接种COVID-19疫苗、BMI为24 kg/cm^{2}以上、合并高血压是患者核酸检测转阴时间延长的独立影响因素。一方面,现阶段奥密克戎变异株虽传染性强,但毒力较前降低,感染者以轻型、普通型为主,全民可以根据自身是否出现咳嗽、咳痰、发

热等症状进行自我监测;另一方面,自身免疫防疫系统非常重要,疫苗的普及可能对病毒造成了很大的约束,对人体有保护作用,尤其体现在老年人等自身免疫力较弱的人群,应尽可能足量全程接种COVID-19疫苗。此外,改善肥胖状态、增强个人身体素质对于抵抗病毒感染也比较重要。

本文存在以下局限性:①研究样本量不够大,且为单中心回顾性研究,所得结果需要更多前瞻性、多中心队列研究进一步验证;②由于当时方舱医院的病例周转较快、医护工作量较大,导致部分数据不完善,比如COVID-19疫苗针剂的剂数、接种不同针剂、是否接种加强针等,无法按照这些资料进行深入分析;③本文资料只描述了现象,至于这些因素对病毒清除的机制影响需要后续深入研究。总之,经过三年的疫情防控,通过COVID-19疫苗人群接种等措施,我们已经进入COVID-19疫情防控的新阶段,未来需要重点关注如何进一步提高疫苗的有效性以及保护易感人群等措施,减少感染、减少重症病例。

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