·临床研究·

高龄老人新型冠状病毒感染患者临床特征及检验结果

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【摘 要】 目的 分析高龄老人新型冠状病毒感染患者的临床特征及实验室检验结果,为高龄老人新型冠状病毒感染(COVID-19)的诊治提供参考。**方法** 回顾性分析海军军医大学第一附属医院干部病房2022年12月7日至12月31日收治的73例80岁及以上COVID-19住院患者的临床资料。根据《新型冠状病毒肺炎诊疗方案(试行第九版)》将患者分为轻中型组(34例)与重危型组(39例),比较2组患者入院时及入院48 h内检验结果。采用SPSS 26.0统计软件进行数据分析。根据数据类型,分别采用t检验、Mann-Whitney U检验或χ^2检验进行组间比较。采用多因素logistic回归分析高龄COVID-19患者出现重症、危重症的影响因素。**结果** 重危型组在院前居家治疗时间、合并慢性基础疾病数量及临床症状数量方面明显高于轻中型组;未吸氧经皮指脉氧饱和度(SpO_2)低于轻中型组,差异均有统计学意义($P<0.05$)。重危型组淋巴细胞计数、淋巴细胞百分比、白蛋白、肾小球滤过率(GFR)、SpO_2、氧分压(PO_2)低于轻中型组;纤维蛋白原、D-二聚体,肌酐、尿素氮、乳酸脱氢酶高于轻中型组,差异均有统计学意义($P<0.05$)。Logistic回归分析结果显示,院前居家治疗时间($OR=0.265$,95%CI 0.085~0.830)与未吸氧SpO_2($OR=1.717$,95%CI 1.016~2.901)是高龄老人发生重症、危重症COVID-19感染的独立危险因素。**结论** 院前居家治疗时间长、未吸氧SpO_2降低的高龄老人是重型或危重型COVID-19的高危人群,应关注其淋巴细胞计数及百分比、凝血功能、肝肾功能、心肌酶谱、动脉血气分析等相关指标等的变化情况,尽早干预,改善预后。

【关键词】 冠状病毒;新型冠状病毒感染;高龄老人
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Clinical characteristics and laboratory test results of elderly patients with coronavirus disease 2019

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【Abstract】 Objective To investigate the clinical characteristics and test results of the elderly patients with coronavirus disease 2019 so as to provide reference for their diagnosis and treatment. **Methods** A retrospective analysis was conducted of the clinical data of 73 COVID-19 inpatients over 80 years old treated in the Cadre's Ward of First Affiliated Hospital of Naval Medical University from December 7 to December 31, 2022. According to COVID-19 Diagnosis and Treatment Protocol (9^{th} Trial Version), the patients were divided into the light and medium group ($n=34$) and the severe and critical group ($n=39$). The test results on admission and 48 h later were compared. SPSS statistics 26.0 was used for data analysis. Data comparison between two groups was performed using t test, Mann-Whitney U test or χ^2 test depending on the data type. Multivariate logistic regression was employed to analyze the independent risk factors for the severe and critical COVID-19 in the elderly. **Results** The severe and critical group had longer pre-hospital home treatment and larger number of underlying comorbid chronic diseases but lower saturation of blood oxygen (SpO_2) without oxygen inhalation than the light and medium group, the differences being statistally significant ($P<0.05$). Lymphocyte count, lymphocyte percentage, albumin, glomeruar filtration rate (GFR), SpO_2 and partial pressure of oxygen (PO_2) in the severe and critical group were lower than those in the light and medium group, and fibrinogen, D-dimer, creatinine, urea nitrogen and lactate dehydrogenase in the former were higher than those in the latter, and the differences were statistically significant. Logistic regression analysis showed that the pre-hospital home treatment time ($OR=0.265$, 95%CI 0.085-0.830) and SpO_2 without oxygen inhalation ($OR=1.717$, 95%CI 1.016-2.901) were the independent risk factors of the severe and critical COVID-19 infection in the elderly. **Conclusion** The elderly with long pre-hospital treatment and low SpO_2 without oxygen inhalation are the high-risk groups for severe or critical COVID-19 infection. Attention should be paid to the changes in lymphocyte count and percentage, coagulation, liver and kidney function, myocardial zymogram, arterial blood gas analysis and other indicators, and intervetion should be taken as soon as possible to improve the prognosis.

【Key words】 corona virus; Covid-19 infection; advanced age
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2022 年 12 月 7 日出台《进一步优化落实新冠肺炎疫情防控的措施》后,新型冠状病毒奥密克戎(Omicron)变异株在人群中出现了快速、广泛的传播,合并多种基础疾病、未接种新冠疫苗的老年人成为高风险人群[1,2]。年龄是新型冠状病毒感染(coronavirus disease 2019,COVID-19)的重要独立危险因素已被大量研究证实[3,4],但对于 80 岁及以上高龄老人 COVID-19 相关研究报道较少。本研究回顾性分析了 73 例 80 岁及以上 COVID-19 住院患者的临床资料,旨在为 COVID-19 的高龄患者提供诊治经验。

1 对象与方法

1.1 研究对象

回顾性分析海军军医大学第一附属医院干部病房 2022 年 12 月 7 日至 2022 年 12 月 31 日收治的 73 例 COVID-19 住院患者的临床资料,其中男性 64 例,女性 9 例;年龄 80~101(92.11±4.02)岁;69 例(94.52%)合并慢性基础疾病。纳入标准:(1)入院前进行咽拭子采样,使用实时荧光反转录聚合酶链反应(reverse transcription-polymerase chain reaction,RT-PCR)法进行新型冠状病毒核酸检测,结果为阳性;(2)年龄≥80 岁;(3)均未接种新冠疫苗。排除标准:治疗期间因其他原因转院。根据《新型冠状病毒肺炎诊疗方案(试行第九版)》[5](简称《方案》)将患者分为轻型、中型、重型与危重型,并将轻型及中型新冠患者列为轻中型组(34 例),全部治愈出院;重型及危重型患者列为重危型组(39 例),治愈 29 例(74.36%),死亡 10 例(25.64%)。

1.2 治疗方案

入院后所有患者的治疗均按照《方案》并结合患者临床病情变化调整,包括一般治疗,抗病毒治疗[奈马特韦片/利托那韦片,52 例患者肾小球滤过率(glomerular filtration rate,GFR)>30 ml/(min · 1.73 m^2),按说明书给药;21 例患者因 GFR<30 ml/(min · 1.73 m^2)未用药],免疫治疗[对于氧合指标进行性恶化、影像学进展、机体炎症反应过度激活的重危患者给予甲基强的松龙 40 mg 静脉注射或地塞米松 6 mg/d 口服,酌情减量,使用时间 3~14 d 不等;对于不适用于奈玛特韦/利托那韦,白细胞介素 6(interleukin-6,IL-6)升高的患者给与托珠单抗 400 mg 静滴]及其他对症支持治疗。

1.3 观察指标

基本资料包括年龄、体质量指数(body mass index,BMI)、未吸氧经皮指脉氧饱和度(saturation of blood oxygen, SpO_2)、院前居家治疗时间(即核酸检测或自测抗原阳性起,至入院治疗的时间),合并慢性基础疾病数量(心脑血管疾病、呼吸系统疾病、2 型糖尿病、肝肾功能不全、恶性肿瘤)。6 项化验检查,包括血常规、C 反应蛋白(C-reactive protein,CRP)、降钙素原(procalcitonin,PCT)、生化指标(肝肾功能、心肌酶、肾功能、电解质等)、凝血功能、动脉血气等。

1.4 统计学处理

采用 SPSS 26.0 统计软件进行数据分析。符合正态分布的计量资料以均数±标准差($\bar{x}\pm s$)表示,组间比较采用 t 检验;不符合正态分布的计量资料使用中位数(四分位数间距)[$M(Q_1, Q_3)$]表示,组间比较采用 Mann-Whitney U 检验。计数资料以例数(百分率)表示,组间比较采用 χ^2 检验。应用多因素 logistic 回归分析高龄 COVID-19 患者重症危重症的危险因素,通过受试者工作特征(receiver operating characteristic,ROC)曲线下面积(area under the curve,AUC)评价模型的区分能力。采用 Hosmer-Lemeshow 拟合优度检验评估模型拟合值与实际值的拟合程度。P<0.05 为差异有统计学意义。

2 结 果

2.1 2 组患者临床资料比较

入院时采集 2 组患者基础临床资料,其中重危型组年龄、院前居家治疗时间、合并慢性基础疾病数量、临床症状数量均高于轻中型组,未吸氧 SpO_2 低于轻中型组,差异均有统计学意义(P<0.05;表 1)。

2.2 多因素 logistic 回归分析高龄老人新型冠状病毒感染的危险因素

将单因素分析中差异有统计学意义的指标(P<0.05)纳入多因素 logistic 回归分析,结果显示重危型高龄老人新型冠状病毒感染患者的独立危险因素为院前居家治疗时间与未吸氧 SpO_2(P<0.05;表 2)。其多因素 logistic 回归模型的 ROC 曲线 AUC = 0.994,95% CI 0.982 ~ 1.005,且具有较高的拟合程度(Hosmer-Lemeshow 拟合优度检验,χ^2 = 0.836,P = 0.999;图 1)。

表 1 2 组患者临床资料比较

Table 1 Comparison of clinical data between two groups

Item	Total (n=73)	Light and medium group (n=34)	Severe and critical group (n=39)	P value
>90 years old[n(%)]	56(76.71)	22(39.29)	34(60.71)	0.023
BMI(kg/m^2, $\bar{x}\pm s$)	23.35±3.79	24.08±4.39	22.71±3.1	0.124
Pre-hospital home treatment time(d, $\bar{x}\pm s$)	3.58±3.91	1.59±0.96	5.33±4.62	<0.001
SpO_2[%, $M(Q_1, Q_3)$]	96(92,97)	97(96,98)	92(90,96)	<0.001
Chronic basic diseases[n, $M(Q_1, Q_3)$]	2(2,3)	2(1,2)	3(2,3)	<0.001
Clinical symptoms[n, $M(Q_1, Q_3)$]	4(3,5)	3(3,4)	5(5,6)	<0.001

BMI: body mass index; SpO_2: saturation of blood oxygen.

2.3 2组患者各项检验指标比较

入院后48 h内留取血标本送检，其中轻中型组在淋巴细胞计数、淋巴细胞百分比、白蛋白、GFR、SpO_2、氧分压(partial pressure of oxygen，PO_2)方面均高于重危型组，在纤维蛋白原、D-二聚体，肌酐、尿素氮、乳酸脱氢酶方面低于重危型组，差异有统计学意义($P<0.05$；表3)。

表2 多因素logistic回归分析高龄老人新型冠状病毒感染患者的危险因素

Table 2 Multivariate logistic regression analysis of risk factors in elderly patients with novel coronavirus infection

Factor	β	*OR*	95%*CI*	*P* value
>90 years old	−5.874	0.003	0.000−6.986	0.141
Pre-hospital home treatment time	−1.328	0.265	0.085−0.830	0.023
SpO_2	0.541	1.717	1.016−2.901	0.043
Chronic basic diseases	−26.152	0.000	0.000−null	0.995
Clinical symptoms	17.193	29300351.270	0.000−null	0.997

SpO_2: saturation of blood oxygen.

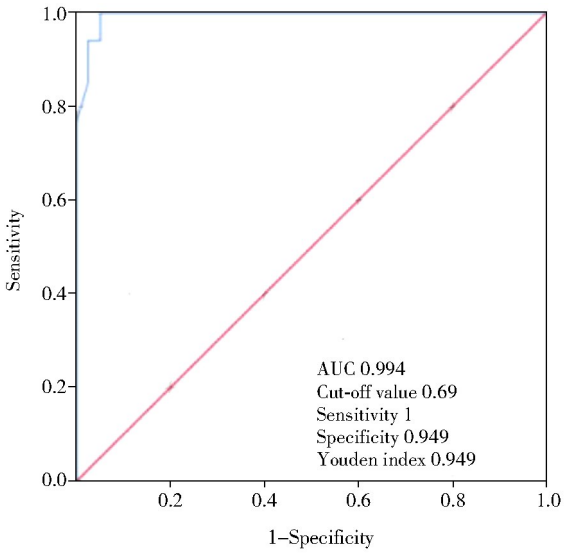

图1 预测模型的ROC曲线

Figure 1 ROC curve of prediction model

ROC: receiver operating characteristic; AUC: area under the curve.

表3 轻中型组与重危型组患者各项检验结果比较

Table 3 Comparison of laboratory examination among the light and medium group and the severe and critical group

Item	Total($n=73$)	Light and medium group($n=34$)	Severe and critical group($n=39$)	*P* value
WBC[$\times10^9$/L, $M(Q_1, Q_3)$]	5.20(4.09,6.69)	5.05(4.01,6.69)	5.40(4.16,7.35)	0.554
NEU[%, $M(Q_1, Q_3)$]	70.00(60.50,75.15)	67.05(59.23,74.20)	70.70(61.70,77.90)	0.175
LYM[$\times10^9$/L, $M(Q_1, Q_3)$]	0.91(0.65,1.12)	1.10(0.87,1.22)	0.71(0.56,0.95)	<0.001
LYM[%, $M(Q_1, Q_3)$]	16.29(12.00,22.78)	19.99(14.87,27.54)	13.89(10.26,20.03)	0.001
CRP(mg/L, $\bar{x}\pm s$)	11.59±17.08	12.38±19.53	10.90±14.85	0.973
PCT[ng/ml, $M(Q_1, Q_3)$]	0.02(0.02,0.11)	0.02(0.02,0.09)	0.02(0.02,0.14)	0.232
Hb(g/L, $\bar{x}\pm s$)	116.85±17.95	120.44±20.74	113.72±14.68	0.111
FIB[g/L, $M(Q_1, Q_3)$]	3.42(2.42,4.42)	2.93(2.17,3.69)	4.08(2.89,4.70)	0.018
D-dimer[mg/L, $M(Q_1, Q_3)$]	1.26(0.54,2.07)	0.94(0.49,1.61)	1.55(0.76,2.62)	0.014
ALB(g/L, $\bar{x}\pm s$)	32.97±4.59	35.10±2.98	31.12±4.96	<0.001
ALT[U/L, $M(Q_1, Q_3)$]	21.00(15.00,34.00)	21.00(14.75,30.00)	23.00(15.00,47.00)	0.525
AST[U/L, $M(Q_1, Q_3)$]	33.00(23.50,46.50)	27.50(21.25,43.50)	35.00(25.00,64.00)	0.058
Cr[μmol/L, $M(Q_1, Q_3)$]	87.00(72.00,124.00)	81.50(66.00,110.50)	113.00(76.00,145.00)	0.034
BUN[mmol/L, $M(Q_1, Q_3)$]	8.60(6.35,12.65)	7.65(5.68,10.65)	9.70(7.00,14.10)	0.031
UA[μmol/L, $M(Q_1, Q_3)$]	279.00(229.00,400.00)	271.00(211.50,394.00)	286.00(237.00,413.00)	0.452
GFR(ml/min, $\bar{x}\pm s$)	44.21±19.67	51.52±19.70	37.85±17.52	0.002
BG[mmol/L, $M(Q_1, Q_3)$]	6.90(5.55,8.75)	6.95(5.95,9.25)	6.50(5.50,8.10)	0.317
K(mmol/L, $\bar{x}\pm s$)	4.06±0.49	4.09±0.43	4.03±0.55	0.111
Na[mmol/L, $M(Q_1, Q_3)$]	131.00(136.00,139.80)	135.10(129.83,138.78)	137.00(131.50,142.00)	0.182
Cl[mmol/L, $M(Q_1, Q_3)$]	96.05(100.60,104.95)	99.50(93.00,103.13)	101.50(97.00,106.00)	0.111
LDH[U/L, $M(Q_1, Q_3)$]	214.00(181.00,300.00)	198.00(175.25,236.75)	245.00(190.00,356.00)	0.018
Mb[ng/ml, $M(Q_1, Q_3)$]	23.78(20.00,109.01)	21.89(20.00,104.10)	46.90(20.00,178.28)	0.454
cTnI[ng/ml, $M(Q_1, Q_3)$]	0.10(0.10,0.20)	0.10(0.10,0.18)	0.14(0.10,0.20)	0.171
NT-proBNP[pg/ml, $M(Q_1, Q_3)$]	1960.90(880.25,4485.20)	1627.10(834.43,2806.85)	2459.20(961.30,5255.00)	0.176
pH($\bar{x}\pm s$)	7.44±0.05	7.43±0.03	7.45±0.05	0.067
SpO_2[%, $M(Q_1, Q_3)$]	97.20(93.85,98.90)	98.45(95.25,99.15)	95.50(91.20,98.50)	0.003
PCO_2[mmHg, $M(Q_1, Q_3)$]	37.43(34.51,41.02)	37.30(34.71,40.65)	37.80(34.43,42.83)	0.678
PO_2[mmHg, $M(Q_1, Q_3)$]	102.42(84.91,126.63)	115.04(101.48,145.68)	87.11(81.74,110.90)	<0.001
Lac(mmol/L, $\bar{x}\pm s$)	1.50(1.10,2.45)	1.55(1.08,2.50)	1.50(1.10,2.40)	0.881

WBC: white blood cell; NEU: neutrophilic granulocyte; LYM: lymphocyte; CRP: C-reactive protein; PCT: procalcitonin; Hb: hemoglobin; FIB: fibrinogen; ALB: albumin; ALT: alanine transaminase; AST: aspartate aminotransferase; Cr: creatinine; BUN: blood urea nitrogen; UA: uric acid; GFR: glomerular filtration rate; BG: blood glucose; LDH: lactate dehydrogenase; Mb: myoglobin; cTnI: cardiac troponin I; NT-proBNP: N-terminal pro-B-type natriuretic peptide; SpO_2: saturation of blood oxygen; PCO_2: partial pressure of carbon dioxide; PO_2: partial pressure of oxygen; Lac: lactic acid. 1 mmHg=0.133 kPa.

3 讨 论

新型冠状病毒 Omicron 变异株具有传染性强、传播速度快、隐匿性强等特点[6]。60 岁及以上老年人、合并慢性基础疾病、BMI≥30 kg/m^2、重度吸烟等因素是 COVID-19 的高危人群[5]。本次入组患者具有以下特点:(1)确诊年龄均≥80 岁,普遍存在免疫力弱、身体机能下降、营养不足等特征;(2)合并慢性基础疾病多;(3)均未接种新冠疫苗;(4)重型/危重型患者比例高;(5)根据 2022 年 12 月上海市新型冠状病毒流行病史,考虑为奥密克戎变异株可能性大。本研究结果显示,患者起病后来院就诊越晚,未吸氧 SpO_2 越低,则出现重症/危重症的可能性越大,也提示高龄老年患者感染 COVID-19 后需要尽早治疗干预,可以减少发展为重症危重症的风险,对疾病转归具有重要意义。

重型/危重型患者淋巴细胞计数、淋巴细胞百分比明显低于轻/中型患者。这可能涉及多个免疫机制,包括病毒直接感染破坏淋巴细胞[7],过度的细胞因子风暴导致淋巴细胞大量消耗并产生免疫抑制[8],病毒的 S 蛋白引起淋巴细胞减少[9,10]等。有研究认为,外周血淋巴细胞计数降低已成为重型、危重型新型冠状病毒肺炎的临床预警指标之一[11]。重危型组纤维蛋白原和 D-二聚体高于轻中型组,这与过去对新型冠状病毒肺炎的研究相符[12,13]。此外,COVID-19 使患者处于高凝状态,增加了静脉血栓栓塞(venous thromboembolism,VTE)风险,可能成为导致患者多器官功能衰竭的原因之一[14]。

重危症组白蛋白水平明显低于轻中型组,心、肾等器官功能指标高于轻中型组,提示营养状况下降可能导致免疫功能下降从而增加重症风险,同时有多项研究表明,COVID-19 会造成心、肺、肝、肾等多器官的免疫损伤,甚至功能衰竭[15]。

本研究也存在一些不足。作为一项回顾性分析,由于病例数有限,缺少如白介素-6 等部分实验室检验结果,且血常规、生化等检验为患者居家治疗(3.58±3.91)d 后入院时留取,因此未纳入多因素 logistics 回归分析。另外由于科室特性,入组病例中女性明显少于男性,因此无法判断性别对 COVID-19 病情发展的影响,也可能导致研究数据有所偏倚。

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