

# 无创正压通气与经鼻高流量氧疗对新型冠状病毒肺炎合并 ARDS 患者临床疗效的影响

赵志伶<sup>1</sup> 曹红<sup>2</sup> 程秦<sup>3</sup> 李楠<sup>4</sup> 张水生<sup>5</sup> 葛庆岗<sup>1</sup> 沈宁<sup>3</sup> 杨林承<sup>6</sup> 史尉利<sup>7</sup>  
白洁<sup>8</sup> 孟庆阳<sup>7</sup> 吴超<sup>9</sup> 王奔<sup>10</sup> 李秋钰<sup>3</sup> 么改琦<sup>1</sup>

<sup>1</sup>北京大学第三医院危重医学科,北京 100191; <sup>2</sup>华中科技大学同济医学院附属同济医院综合科,湖北武汉 430030; <sup>3</sup>北京大学第三医院呼吸与危重症医学科,北京 100191; <sup>4</sup>北京大学第三医院临床流行病学研究中心,北京 100191; <sup>5</sup>北京大学第三医院普通外科,北京 100191; <sup>6</sup>北京大学第三医院心内科,北京 100191; <sup>7</sup>北京大学第三医院运动医学研究所,北京 100191; <sup>8</sup>北京大学第三医院胸外科,北京 100191; <sup>9</sup>北京大学第三医院神经外科,北京 100191; <sup>10</sup>北京大学第三医院骨科,北京 100191

通信作者:葛庆岗, Email: qinggangelin@126.com

**【摘要】** 目的 观察无创正压通气(NIPPV)和经鼻高流量氧疗(HFNC)对新型冠状病毒肺炎(新冠肺炎)合并急性呼吸窘迫综合征(ARDS)患者预后的影响。方法 采用回顾性研究方法,选择2020年2月至4月作者援鄂期间在华中科技大学同济医学院附属同济医院收治的脉搏血氧饱和度/吸入氧浓度比值( $SpO_2/FiO_2$ , S/F) < 235 [利用S/F比值代替氧合指数( $PaO_2/FiO_2$ )诊断ARDS]的新冠肺炎患者。按氧疗模式不同将患者分为NIPPV组和HFNC组。收集患者的临床资料,包括:一般特征、呼吸频率(RR)、 $FiO_2$ 、 $SpO_2$ 、心率(HR)、平均动脉压(MAP),最初72 h S/F比值、入院/出院前/死亡前淋巴细胞计数(LYM)、淋巴细胞比例(LYM%)、白细胞计数(WBC)、通气前呼吸困难病程、发病至入院时间等,比较不同氧疗模式患者需要插管率、全因病死率、S/F比值和RR改善情况的差异。采用单因素分析和广义估计方程(GEE)方法分析影响S/F比值的危险因素。结果 41例患者中男性比例较高(占68.3%, 28例),中位年龄68(58~74)岁,28例有合并症(占68.3%),发生多器官功能障碍综合征(MODS)34例(占82.9%)。与HFNC组比较,NIPPV组合并症更多[87.5%(21/24)比41.2%(7/17),  $P < 0.05$ ], LYM%更低[5.3%(3.4%~7.8%)比10.0%(3.9%~19.7%),  $P < 0.05$ ], 血液净化治疗率也更低[0%(0/24)比29.4%(5/17),  $P < 0.05$ ]。随时间延长,NIPPV组治疗2 h后S/F比值逐渐升高,RR逐渐下降;HFNC组S/F比值较基线有下降趋势,两组各时间点S/F比值比较差异均无统计学意义,而RR则较基线有上升趋势,治疗2 h NIPPV组RR明显高于HFNC组[次/min: 30(27~33)比24(21~27),  $P < 0.05$ ]。NIPPV组与HFNC组需要插管率和病死率比较差异均无统计学意义[66.7%(16/24)比70.6%(12/17), 58.3%(14/24)比52.9%(9/17), 均 $P > 0.05$ ]。分析影响氧疗过程中S/F比值的因素显示:氧疗方式和入院时病程是影响患者S/F比值的因素[ $\beta$ 值分别为-15.827、1.202, 95%可信区间(95%CI)分别为-29.102~-2.552和0.247~2.156,  $P$ 值分别为0.019、0.014]。结论 与HFNC相比,NIPPV未显著降低新冠肺炎合并ARDS患者的需要插管率和病死率,但可显著提高新冠肺炎患者的S/F比值。

**【关键词】** 无创正压通气; 经鼻高流量氧疗; 新型冠状病毒肺炎; 急性呼吸窘迫综合征

基金项目:北京大学医学部交叉种子基金项目(BMU2021MX020)

DOI: 10.3760/cma.j.cn121430-20210104-00002

## Effect of noninvasive positive pressure ventilation and high-flow nasal cannula oxygen therapy on the clinical efficacy of coronavirus disease 2019 patients with acute respiratory distress syndrome

Zhao Zhiling<sup>1</sup>, Cao Hong<sup>2</sup>, Cheng Qin<sup>3</sup>, Li Nan<sup>4</sup>, Zhang Shuisheng<sup>5</sup>, Ge Qinggang<sup>1</sup>, Shen Ning<sup>3</sup>, Yang Lincheng<sup>6</sup>, Shi Weili<sup>7</sup>, Bai Jie<sup>8</sup>, Meng Qingyang<sup>7</sup>, Wu Chao<sup>9</sup>, Wang Ben<sup>10</sup>, Li Qiuyu<sup>3</sup>, Yao Gaiqi<sup>1</sup>

<sup>1</sup>Department of Intensive Care Unit, Peking University Third Hospital, Beijing 100191, China; <sup>2</sup>Department of Geriatrics, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan 430030, Hubei, China; <sup>3</sup>Department of Respiratory and Critical Care Medicine, Peking University Third Hospital, Beijing 100191, China; <sup>4</sup>Department of Research Center of Clinical Epidemiology, Peking University Third Hospital, Beijing 100191, China; <sup>5</sup>Department of General Surgery, Peking University Third Hospital, Beijing 100191, China; <sup>6</sup>Department of Cardiology, Peking University Third Hospital, Beijing 100191, China; <sup>7</sup>Department of Institute of Sports Medicine, Peking University Third Hospital, Beijing 100191, China; <sup>8</sup>Department of Thoracic Surgery, Peking University Third Hospital, Beijing 100191, China; <sup>9</sup>Department of Neurosurgery, Peking University Third Hospital, Beijing 100191, China; <sup>10</sup>Department of Orthopedics, Peking University Third Hospital, Beijing 100191, China

Corresponding author: Ge Qinggang, Email: qinggangelin@126.com

**【Abstract】 Objective** To observe the effect of noninvasive positive pressure ventilation (NIPPV) and high-flow nasal cannula oxygen therapy (HFNC) on the prognosis of patients with coronavirus disease 2019 (COVID-19) accompanied with acute respiratory distress syndrome (ARDS). **Methods** A retrospective study was conducted in Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology when authors worked as medical team members for treating COVID-19. COVID-19 patients with pulse oxygen saturation/fraction of inspiration oxygen ( $SpO_2/FiO_2$ , S/F) ratio < 235, managed by medical teams [using S/F ratio instead of oxygenation index ( $PaO_2/FiO_2$ ) to diagnose ARDS] from February to April 2020 were included. The patients were divided into NIPPV group and HFNC group according to their oxygen therapy modes. Clinical data of patients were collected, including general characteristics, respiratory rate (RR), fraction of  $FiO_2$ ,  $SpO_2$ , heart rate (HR), mean arterial pressure (MAP), S/F ratio in the first 72 hours, lymphocyte count (LYM), percentage of lymphocyte (LYM%) and white blood cell count (WBC) at admission and discharge or death, the duration of dyspnea before NIPPV and HFNC, and the length from onset to admission. The differences of intubation rate, all-cause mortality, S/F ratio and RR were analyzed, and single factor analysis and generalized estimation equation (GEE) were used to analyze the risk factors affecting S/F ratio. **Results** Among the 41 patients, the proportion of males was high (68.3%, 28 cases), the median age was 68 (58–74) years old, 28 cases had complications (68.3%), and 34 cases had multiple organ dysfunction syndrome (MODS, 82.9%). Compared with HFNC group, the proportion of complications in NIPPV group was higher [87.5% (21/24) vs. 41.2% (7/17),  $P < 0.05$ ], and the value of LYM% was lower [5.3% (3.4%–7.8%) vs. 10.0% (3.9%–19.7%),  $P < 0.05$ ], the need of blood purification was also significantly lower [0% (0/24) vs. 29.4% (5/17),  $P < 0.05$ ]. The S/F ratio of NIPPV group gradually increased after 2 hours treatment and RR gradually decreased with over time, S/F ratio decreased and RR increased in HFNC group compared with baseline, but there was no significant difference in S/F ratio between the two groups at each time point. RR in NIPPV group was significantly higher than that in HFNC group after 2 hours treatment [time/min: 30 (27–33) vs. 24 (21–27),  $P < 0.05$ ]. There was no significant difference in rate need intubation and hospital mortality between NIPPV group and HFNC group [66.7% (16/24) vs. 70.6% (12/17), 58.3% (14/24) vs. 52.9% (9/17), both  $P > 0.05$ ]. Analysis of the factors affecting the S/F ratio in the course of oxygen therapy showed that the oxygen therapy mode and the course of illness at admission were the factors affecting the S/F ratio of patients [ $\beta$  values were -15.827, 1.202, 95% confidence interval (95%CI) were -29.102 to -2.552 and 0.247–2.156,  $P$  values were 0.019 and 0.014, respectively]. **Conclusion** Compared with HFNC, NIPPV doesn't significantly reduce the intubation rate and mortality of patients with COVID-19 accompanied with ARDS, but it significantly increases the S/F ratio of those patients.

**【Key words】** Noninvasive positive pressure ventilation; High-flow nasal cannula oxygen therapy; Coronavirus disease 2019; Acute respiratory distress syndrome

**Fund program:** Cross Seed Fund Project of Peking University Medical College (BMU2021MX020)

DOI: 10.3760/cma.j.cn121430-20210104-00002

自新型冠状病毒肺炎(新冠肺炎)在全球暴发以来,病死率高达 15.6%<sup>[1]</sup>,严重威胁人类生命。目前大型临床试验表明,抗病毒药物<sup>[2]</sup>、白细胞介素-6受体拮抗剂<sup>[3]</sup>并未降低新冠肺炎患者病死率,而干细胞<sup>[4]</sup>、康复期血浆<sup>[5]</sup>治疗新冠肺炎并发 ARDS 患者,因纳入病例数量少、混杂因素较多等无法在临床上大规模推广,目前仍无特效药物治疗,而氧疗是重症新冠肺炎患者最基本也最重要的措施,因此重症新冠肺炎患者的最佳氧疗方式一直备受人们的广泛关注。

研究表明,无创正压通气(non-invasive positive pressure ventilation, NIPPV)和经鼻高流量氧疗(high-flow nasal cannula oxygen therapy, HFNC)可以降低非新冠肺炎导致的低氧血症患者插管率<sup>[6-7]</sup>。但目前鲜见有关 NIPPV 和 HFNC 在新冠肺炎难治性低氧血症患者中优越性及安全性比较的研究。本研究通过观察 NIPPV 和 HFNC 对新冠肺炎并发急性呼吸窘迫综合征(acute respiratory distress

syndrome, ARDS)患者临床疗效的影响,以期为临床治疗新冠肺炎提供参考。

## 1 资料与方法

**1.1 研究对象:**采用回顾性研究方法,收集 2020 年 2 月至 4 月作者援鄂期间在华中科技大学同济医学院附属同济医院收治的新冠肺炎并发 ARDS 接受 NIPPV 和 HFNC 患者的临床资料。由于新冠肺炎发病初期动脉血气值缺乏,因此,脉搏血氧饱和度/吸入氧浓度比值[pulse oxygen saturation/fraction of inspiration oxygen,  $SpO_2/FiO_2$  (S/F)]被用于替代诊断 ARDS 的氧合指数( $PaO_2/FiO_2$ )<sup>[8-9]</sup>。

**1.1.1 纳入标准:**① S/F 比值 < 235,符合 ARDS 诊断;② 应用 NIPPV 和 HFNC > 12 h/d;③ 年龄 > 18 岁。

**1.1.2 排除标准:**① 入院后 24 h 死亡;② 血流动力学不稳定;③ 格拉斯哥昏迷评分(Glasgow coma scale, GCS)评分 < 12 分;④ 不能耐受 NIPPV 和 HFNC;⑤ 存在谵妄;⑥ 氧疗资料不完整。

**1.1.3 伦理学:**本研究符合医学伦理学标准,并

经北京大学第三医院伦理委员会批准(审批号: 2020-047-01),对患者采取的治疗和检测均参照实时新冠肺炎诊疗方案。

**1.2 研究分组:**将患者按氧疗模式不同分为 NIPPV 组和 HFNC 组。

**1.3 氧疗方案:**① NIPPV 方案:在一定程度上支持压力取决于患者耐受性,压力和 FiO<sub>2</sub> 滴定至 SpO<sub>2</sub> ≥ 0.94, NIPPV 患者在进食时给予经鼻导管吸氧;② HFNC 方案:经鼻导管持续给予高流量湿化的氧气(37 °C, 44 cmH<sub>2</sub>O/L),最初流速设定为 50 L/min,如果可能可上调至 70 L/min,最初 FiO<sub>2</sub> 为 0.70,后续调整根据目标值维持 SpO<sub>2</sub> ≥ 0.94。

**1.4 气管插管指征**<sup>[10-11]</sup>:① 患者血流动力学不稳定或心电不稳定;② 意识状态恶化;③ 存在以下至少 2 条以上呼吸衰竭(呼衰)持续存在或恶化的表现:呼吸频率(respiratory rate, RR) > 40 次/min;呼吸肌负荷过重无明显改善;气道分泌物明显增多;酸中毒:pH 值 < 7.35;吸入纯氧的条件下 SpO<sub>2</sub> < 0.90 在 5 min 以上。

**1.5 资料收集:**查阅电子病历系统、特护记录及实验室检查报告,收集患者一般特征、合并症、心率(heart rate, HR)、平均动脉压(mean arterial pressure, MAP)、RR、FiO<sub>2</sub>、SpO<sub>2</sub>、NIPPV 和 HFNC 最初 72 h S/F 比值,患者入院时和出院前或死亡前淋巴细胞计数(lymphocyte count, LYM)、淋巴细胞比例(percentage of lymphocytes, LYM%)及白细胞计数(white blood cell count, WBC), NIPPV 和 HFNC 前呼吸困难时间以及入院前病程。分析并比较 NIPPV

组和 HFNC 组患者主要研究结局(插管率、插管前 NIPPV 或 HFNC 时间、插管原因、全因病死率、死亡原因)、S/F 比值和 RR,以及插管前病程、次要研究结局[血液净化治疗率、器官功能衰竭和多器官功能障碍综合征(multiple organ dysfunction syndrome, MODS)发生率]的差异。

**1.6 统计学分析:**使用 SPSS 26.0 统计软件分析数据。由于小样本量评估连续变量正态性的困难,因此以中位数(范围)[M(范围)]来描述连续变量,采用非参数检验。分类变量以例(%)表示,采用  $\chi^2$  检验。采用广义估计方程(generalized estimation equation, GEE)分析吸氧过程中氧疗方式与 S/F 比值的关系。 $P < 0.05$  为差异有统计学意义。

**2 结果**

**2.1 新冠肺炎患者入院时基线特征和一般资料**(表 1):共收治 69 例新冠肺炎并发 ARDS 患者,其中实施 NIPPV 46 例, HFNC 患者 17 例,面罩给氧 6 例。46 例 NIPPV 患者中排除 22 例:NIPPV 治疗前休克 3 例,昏迷 3 例, NIPPV 不能耐受 5 例, NIPPV < 4 h 3 例, S/F 比值 ≥ 235 1 例, NIPPV 电子病历缺失 6 例,入院后 24 h 内死亡 1 例。最后纳入患者 NIPPV 组 24 例和 HFNC 组 17 例。41 例患者大多数为男性, 28 例有合并症。NIPPV 组合并症比例明显高于 HFNC 组 [87.5% (21/24) 比 41.2% (7/17),  $P < 0.05$  ], LYM% 明显低于 HFNC 组 ( $P < 0.05$ )。两组性别、年龄、入院前病程、治疗前呼吸困难时间、LYM、WBC、HR、MAP、RR 和 S/F 比值比较差异均无统计学意义(均  $P > 0.05$ )。

表 1 不同氧疗模式两组新型冠状病毒肺炎并发 ARDS 患者基线特征比较

组别	例数 (例)	性别(例)		年龄 [岁, M(范围)]	合并症[例(%)]					入院前病程 [d, M(范围)]	治疗前呼吸困难时间 [d, M(范围)]
		男性	女性		糖尿病	高血压	心血管疾病	脑血管疾病	COPD		
全体	41	28	13	68(58~74)	9(22.0)	20(48.8)	3(7.3)	4(9.8)	4(9.8)	10.0(7.5~14.5)	11.0(7.0~15.0)
NIPPV 组	24	18	6	68(62~76)	7(29.2)	14(58.3)	1(4.2)	2(8.3)	2(8.3)	10.5(7.3~15.0)	10.5(7.0~15.0)
HFNC 组	17	10	7	64(54~74)	2(11.8)	6(35.3)	2(11.8)	2(11.8)	2(11.8)	10.0(7.0~12.0)	11.0(6.5~14.5)
$\chi^2/Z$ 值		1.203		1.165	0.890	2.114	0.097	0.000	0.000	0.917	0.040
P 值		0.273		0.244	0.346	0.146	0.755	1.000	1.000	0.359	0.968
组别	例数 (例)	LYM [×10 <sup>9</sup> /L, M(范围)]		LYM% [% , M(范围)]	WBC [×10 <sup>9</sup> /L, M(范围)]	HR [次/min, M(范围)]	MAP [mmHg, M(范围)]	RR [次/min, M(范围)]	S/F 比值 [M(范围)]		
全体	41	0.56(0.41~0.84)		6.5(3.7~10.4)	8.07(6.03~11.94)	92.0(80.0~108.0)	102.0(88.5~110.0)	27.0(23.0~31.0)	126.23(111.11~141.97)		
NIPPV 组	24	0.55(0.36~0.78)		5.3(3.4~7.8)	9.15(6.90~15.32)	93.0(79.3~107.8)	105.5(89.0~111.5)	28.5(23.0~35.5)	118.03(110.15~131.15)		
HFNC 组	17	0.66(0.42~0.88)		10.0(3.9~19.7)	7.28(4.01~10.65)	90.0(81.0~108.5)	95.0(86.5~107.0)	25.0(22.0~29.0)	131.15(111.11~156.31)		
Z 值		-1.019		-2.130	1.747	-0.252	1.219	1.778	-1.193		
P 值		0.308		0.033	0.081	0.801	0.233	0.075	0.233		

注:ARDS 为急性呼吸窘迫综合征, NIPPV 为无创正压通气, HFNC 为经鼻高流量氧疗, COPD 为慢性阻塞性肺疾病, LYM 为淋巴细胞计数, LYM% 为淋巴细胞比例, WBC 为白细胞计数, HR 为心率, MAP 为平均动脉压, RR 为呼吸频率, S/F 比值为脉搏血氧饱和度/吸入氧浓度比值; 1 mmHg=0.133 kPa



**2.2** NIPPV组和HFNC组新冠肺炎并发ARDS患者不同时间点S/F比值和RR的比较(表2):与HFNC组比较,NIPPV组治疗2、12、24、48、72h S/F比值有升高趋势,但两组比较差异均无统计学意义(均 $P>0.05$ )。而HFNC组治疗2h RR较NIPPV组明显降低,差异有统计学意义( $P<0.05$ ),两组其余各时间点RR比较差异均无统计学意义(均 $P>0.05$ )。

**表2** 不同氧疗模式两组新型冠状病毒肺炎并发ARDS患者呼吸参数比较

组别	时间	S/F比值		RR	
		例数 (例)	数值 [M(范围)]	例数 (例)	数值 [次/min, M(范围)]
NIPPV组	基线	24	118.03(110.15~131.15)	24	29(23~36)
	2h	24	118.01(97.27~154.39)	24	30(27~33)
	12h	23	125.29(110.41~159.58)	23	31(27~35)
	24h	22	129.59(114.65~150.00)	22	24(20~29)
	48h	21	130.26(100.08~159.52)	21	23(20~31)
	72h	19	134.28(119.75~188.00)	19	24(21~29)
HFNC组	基线	17	131.15(111.11~156.31)	17	25(22~29)
	2h	17	115.00(94.97~140.71)	17	24(21~27) <sup>a</sup>
	12h	17	116.05(94.96~132.14)	17	24(22~34)
	24h	16	121.11(95.42~147.14)	16	24(21~32)
	48h	13	115.00(92.41~139.28)	13	24(22~30)
	72h	11	120.99(95.56~140.00)	11	30(24~33)

注:ARDS为急性呼吸窘迫综合征,NIPPV为无创正压通气, HFNC为经鼻高流量氧疗,S/F比值为脉搏血氧饱和度/吸入氧浓度比值,RR为呼吸频率;与NIPPV组同期比较,<sup>a</sup> $P<0.05$

**2.3** 影响新冠肺炎并发ARDS患者氧疗过程中S/F比值的因素分析(表3):剔除缺失数据的个体后,共有184组资料(占205组资料总数的89.8%)被用于构建GEE模型。GEE结果显示,在控制其他因素后,入院时的氧疗方式及病程是影响S/F比值的因素。入院前病程越长,氧疗后S/F比值改善越好。

**表3** 基于GEE影响新型冠状病毒肺炎并发ARDS患者氧疗过程中S/F比值的因素分析

参数	$\beta$ 值	$\chi^2$ 值	95%CI	P值
HFNC(以NIPPV为参考)	-15.827	5.460	-29.102~-2.552	0.019
男性(以女性为参考)	-0.753	0.009	-15.884~14.378	0.922
年龄	-0.035	0.009	-0.724~0.655	0.922
MAP	0.327	3.228	-0.030~0.684	0.072
治疗前呼吸困难时间	0.588	0.765	-0.730~1.906	0.382
入院时病程	1.202	6.090	0.247~2.156	0.014
合并症数量	-5.385	1.878	-13.085~2.316	0.171
基线LYM%	-0.287	0.216	-1.498~0.924	0.642
基线WBC	-1.019	0.854	-3.180~1.142	0.355
基线S/F比值	0.205	1.042	-0.188~0.598	0.307
时间点(以72h为参考)				
2h	-15.266	2.917	-32.786~2.253	0.088
12h	-10.996	2.122	-25.792~3.800	0.145
24h	-10.883	2.636	-24.019~2.254	0.104
48h	-7.235	2.277	-16.633~2.163	0.131

注:GEE为广义估计方程,ARDS为急性呼吸窘迫综合征,S/F比值为脉搏血氧饱和度/吸入氧浓度比值, HFNC为经鼻高流量氧疗,NIPPV为无创正压通气,MAP为平均动脉压,LYM%为淋巴细胞比例,WBC为白细胞计数,95%CI为95%可信区间

**2.4** 不同氧疗模式两组新冠肺炎并发ARDS患者主要和次要研究结果比较(表4):两组总病死率为56.1%(23/41)。NIPPV组实际插管率和血液净化治疗率均显著低于HFNC组(均 $P<0.05$ )。两组需要插管率、插管前NIPPV或HFNC时间、需要插管的原因、病死率、死亡原因、插管前病程、器官功能衰竭和MODS发生率比较差异均无统计学意义(均 $P>0.05$ )。

**3 讨论**

新冠肺炎重症患者表现为严重的呼吸困难状和免疫损伤,LYM、CD4<sup>+</sup>下降,白细胞介素-6(interleukin-6, IL-6)显著升高<sup>[12-13]</sup>,透明膜形成和间质单核细胞炎性浸润是其病理特征<sup>[14-15]</sup>。Chopra

**表4** 不同氧疗模式两组新型冠状病毒肺炎并发ARDS患者主要和次要研究结局比较

组别	例数 (例)	实际插管率 [% (例)]	需要插管率 [% (例)]	插管前NIPPV 或HFNC时间 [d, M(范围)]	需要插管的原因[例(%)]		病死率 [% (例)]	死亡原因[例(%)]		
					呼吸衰竭	循环衰竭		难治性 休克	难治性 低氧血症	心搏骤停
NIPPV组	24	37.5(9)	66.7(16)	7.0(2.5~10.5)	15(62.5)	1(4.2)	58.3(14)	1(4.2)	9(37.5)	4(16.7)
HFNC组	17	70.6(12)	70.6(12)	4.5(2.3~9.0)	12(70.6)	0(0)	52.9(9)	1(5.9)	3(17.6)	5(29.4)
$\chi^2/Z$ 值		4.361	0.071	0.107	0.290	0.000	0.117	0.000	1.057	0.346
P值		0.037	0.790	0.971	0.591	1.000	0.732	1.000	0.304	0.556
组别	例数 (例)	插管前病程 [d, M(范围)]	血液净化 治疗率[% (例)]	器官功能衰竭[例(%)]				MODS发生率 [% (例)]		
				肾衰竭	循环系统衰竭	肝衰竭	凝血系统障碍		中枢神经系统障碍	
NIPPV组	24	5.5(4.8~10.8)	0(0)	5(20.8)	14(58.3)	5(20.8)	12(50.0)	2(8.3)	83.3(20)	
HFNC组	17	4.0(2.0~11.0)	29.4(5)	3(17.6)	12(70.6)	3(17.6)	11(64.7)	1(5.9)	82.4(14)	
$Z/\chi^2$ 值		0.107	5.527	0.000	0.644	0.000	0.874	0.000	0.000	
P值		0.917	0.019	1.000	0.422	1.000	0.350	1.000	1.000	

注:ARDS为急性呼吸窘迫综合征,NIPPV为无创正压通气, HFNC为经鼻高流量氧疗,MODS为多器官功能障碍综合征

等<sup>[16]</sup>报道重症新冠肺炎患者病死率高达 62.5%。病情快速进展使重症患者的治疗极具挑战性。早期确定最佳治疗方案,特别是机械通气方式,可以改善由新冠肺炎引起 ARDS 危重患者的预后。但国内以个案报道多见,如郝泉水等<sup>[17]</sup>及何慧洁等<sup>[18]</sup>的研究表明,无创通气失败后积极有创机械通气可改善新冠肺炎患者预后,但目前尚无大宗病例报告。

与文献报告结果相似<sup>[19]</sup>,本研究结果显示,NIPPV 对代表 PaO<sub>2</sub>/FiO<sub>2</sub> 指标的 S/F 改善程度较 HFNC 更优,但 NIPPV 在降低新冠肺炎并发 ARDS 患者的插管率和病死率方面并不优于 HFNC,且需要插管率高达 66.7%,显著高于非新冠肺炎相关 ARDS 患者的无创通气失败率(31.0%~61.5%)<sup>[20-22]</sup>,但与 H1N1 (94%)<sup>[23]</sup>和中东呼吸综合征(57.1%)并发 ARDS<sup>[24]</sup>的 NIPPV 失败率基本相似。本研究显示,HFNC 的需要插管率也高达 70.6%,显著高于急性低氧性呼吸衰竭患者 HFNC 的失败率(21%~55%)<sup>[11,25-28]</sup>,但与 Hernandez-Romieu 等<sup>[29]</sup>报告新冠肺炎患者 HFNC 的失败率相似(71.6%),提示以双肺弥漫性浸润为特征的流行性病毒性疾病 NIPPV 或 HFNC 失败的风险极高。本研究 NIPPV 组实际插管率显著低于 HFNC 组,分析其原因可能与 NIPPV 改善了患者的呼吸症状如 S/F 比值,从而掩盖了病情的进展有关。本研究表明,患者入院时病程越长,氧疗后 S/F 比值改善越好,分析可能与病情进展较慢的患者,肺部病变相对急性起病者较轻有关。

本研究 NIPPV 组和 HFNC 组病死率显著高于文献报道非新冠肺炎相关 ARDS 患者接受 NIPPV 治疗的病死率(35%)<sup>[30]</sup>和 HFNC 的病死率(6.8%~20.0%)<sup>[1,26-27]</sup>。本研究 HFNC 的插管率与 Hernandez-Romieu 等<sup>[29]</sup>报告新冠肺炎 HFNC 的插管率相似,但病死率高于 Hernandez-Romieu 等<sup>[29]</sup>的研究结果,NIPPV 组患者病死率与 Burns 等<sup>[31]</sup>和 Chopra 等<sup>[16]</sup>报告的病死率接近(58.3%比 50%、62.5%),但在 Burns 等<sup>[31]</sup>的研究中患者有更多合并症和更高的器官功能衰竭发生率,而 Chopra 等<sup>[16]</sup>的研究显示,机械通气组有更高的气压伤,认为气压伤作为肺部疾病进展的结果可能是高病死率的重要原因之一。本研究患者 MODS 的发生率高达 82.9%,提示本研究所涉及的患者疾病严重程度较重。难治性低氧血症、LYM 和 LYM% 下降伴随 MODS 及心搏骤停是本研究病死率较高的原因,与文献报道结果相似<sup>[32-35]</sup>。尽管 Hernandez-Romieu 等<sup>[29]</sup>发现,延迟插管与病

死率无关,但此研究延迟插管时间不超过 1 d,而本研究与其他研究<sup>[11]</sup>相比,插管前 NIPPV 或 HFNC 时间显著延长,表明延迟插管可能会导致呼吸机相关性肺损伤、呼吸肌疲劳和氧债务增加<sup>[36-37]</sup>。另外普通病房医护人员对 NIPPV 插管时机的评估能力可能是其失败的另一个重要原因<sup>[38-39]</sup>。ICU 床位不足<sup>[40]</sup>及氧疗设备短缺是各国疫情暴发初期面临的严重问题,增加重症新冠肺炎患者的死亡风险,因此监测 ICU 床位负荷与需求、及时调整 ICU 的床位供应和具备重症监护能力的医务人员数量是降低病死率的重要措施。

综上所述,对新冠肺炎并发 ARDS 患者使用 NIPPV 和 HFNC 应根据反映 PaO<sub>2</sub>/FiO<sub>2</sub> 的 S/F 比值、呼吸困难症状如 RR、辅助呼吸支持水平及器官功能状态等综合评估,在短时间内无明显好转应快速进行气管插管呼吸机辅助通气,减少呼吸肌疲劳和氧债务;同时应加强普通病房医护人员对 NIPPV 和 HFNC 流程、报警的处理能力、插管时机的培训,以便在疫情暴发时快速组建应对重症病情的精锐队伍,才能在疾病早期使患者得到最优化的氧疗方案,从而改善患者预后。

**利益冲突** 所有作者均声明不存在利益冲突

## 参考文献

- [1] Asch DA, Sheils NE, Islam MN, et al. Variation in US hospital mortality rates for patients admitted with COVID-19 during the first 6 months of the pandemic [J]. *JAMA Intern Med*, 2021, 181 (4): 471-478. DOI: 10.1001/jamainternmed.2020.8193.
- [2] Cao B, Wang Y, Wen D, et al. A trial of Lopinavir-Ritonavir in adults hospitalized with severe Covid-19 [J]. *N Engl J Med*, 2020, 382 (19): 1787-1799. DOI: 10.1056/NEJMoa2001282.
- [3] Rosas IO, Bräu N, Waters M, et al. Tocilizumab in hospitalized patients with severe Covid-19 pneumonia [J]. *N Engl J Med*, 2021, 384 (16): 1503-1516. DOI: 10.1056/NEJMoa2028700.
- [4] Iglesias M, Butrón P, Torre-Villalvazo I, et al. Mesenchymal stem cells for the compassionate treatment of severe acute respiratory distress syndrome due to COVID 19 [J]. *Aging Dis*, 2021, 12 (2): 360-370. DOI: 10.14336/AD.2020.1218.
- [5] Hatzl S, Posch F, Sareban N, et al. Convalescent plasma therapy and mortality in COVID-19 patients admitted to the ICU: a prospective observational study [J]. *Ann Intensive Care*, 2021, 11 (1): 73. DOI: 10.1186/s13613-021-00867-9.
- [6] Xu XP, Zhang XC, Hu SL, et al. Noninvasive ventilation in acute hypoxemic nonhypercapnic respiratory failure: a systematic review and Meta-analysis [J]. *Crit Care Med*, 2017, 45 (7): e727-e733. DOI: 10.1097/CCM.0000000000002361.
- [7] Zhao HY, Wang HX, Sun F, et al. High-flow nasal cannula oxygen therapy is superior to conventional oxygen therapy but not to noninvasive mechanical ventilation on intubation rate: a systematic review and meta-analysis [J]. *Crit Care*, 2017, 21 (1): 184. DOI: 10.1186/s13054-017-1760-8.
- [8] World Health Organization. Clinical management of severe acute respiratory infection (SARI) when COVID-19 disease is suspected: interim guidance [EB/OL]. (2020-03-13) [2020-11-04]. <https://apps.who.int/iris/handle/10665/331446>.
- [9] Rice TW, Wheeler AP, Bernard GR, et al. Comparison of the SpO<sub>2</sub>/FIO<sub>2</sub> ratio and the PaO<sub>2</sub>/FIO<sub>2</sub> ratio in patients with acute lung injury or ARDS [J]. *Chest*, 2007, 132 (2): 410-417. DOI: 10.1378/chest.07-0617.

- [10] Antonelli M, Conti G, Rocco M, et al. A comparison of noninvasive positive-pressure ventilation and conventional mechanical ventilation in patients with acute respiratory failure [J]. *N Engl J Med*, 1998, 339 (7): 429-435. DOI: 10.1056/NEJM199808133390703.
- [11] Frat JP, Thille AW, Mercat A, et al. High-flow oxygen through nasal cannula in acute hypoxemic respiratory failure [J]. *N Engl J Med*, 2015, 372 (23): 2185-2196. DOI: 10.1056/NEJMoa1503326.
- [12] 史晓朋, 秦历杰, 杨蕾, 等. 白细胞介素-6联合CD4<sup>+</sup>T淋巴细胞检测对评估新型冠状病毒肺炎严重程度及预后的价值 [J]. *中华危重病急救医学*, 2020, 32 (10): 1165-1170. DOI: 10.3760/cma.j.cn121430-20200521-00395.
- Shi XP, Qin LJ, Yang L, et al. Value of interleukin-6 and CD4<sup>+</sup>T-lymphocytopenia in assessing the severity and prognosis of coronavirus disease 2019 [J]. *Chin Crit Care Med*, 2020, 32 (10): 1165-1170. DOI: 10.3760/cma.j.cn121430-20200521-00395.
- [13] 于洪志, 邵红霞, 邢志珩, 等. 天津地区新型冠状病毒肺炎患者临床特征分析 [J]. *天津医药*, 2020, 48 (7): 577-582. DOI: 10.11958/20201093.
- Yu HZ, Shao HX, Xing ZH, et al. Analysis of clinical characteristics of patients with COVID-19 in Tianjin [J]. *Tianjin Med J*, 2020, 48 (7): 577-582. DOI: 10.11958/20201093.
- [14] Huang CL, Wang YM, Li XW, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China [J]. *Lancet*, 2020, 395 (10223): 497-506. DOI: 10.1016/S0140-6736(20)30183-5.
- [15] Xu Z, Shi L, Wang YJ, et al. Pathological findings of COVID-19 associated with acute respiratory distress syndrome [J]. *Lancet Respir Med*, 2020, 8 (4): 420-422. DOI: 10.1016/S2213-2600(20)30076-X.
- [16] Chopra A, Al-Tarbsheh AH, Shah NJ, et al. Pneumothorax in critically ill patients with COVID-19 infection: incidence, clinical characteristics and outcomes in a case control multicenter study [J]. *Respir Med*, 2021, 184: 106464. DOI: 10.1016/j.rmed.2021.106464.
- [17] 郝泉水, 杨亚东, 贾丽萍, 等. 危重型新型冠状病毒肺炎机械通气患者成功脱机体会 [J]. *中国中西医结合急救杂志*, 2020, 27 (5): 524-527. DOI: 10.3969/j.issn.1008-9691.2020.05.003.
- Hao QS, Yang YD, Jia LP, et al. Successful extubation experience in treatment of a critical patient with coronavirus disease 2019 by tracheal intubation mechanical ventilation [J]. *Chin J TCM WM Crit Care*, 2020, 27 (5): 524-527. DOI: 10.3969/j.issn.1008-9691.2020.05.003.
- [18] 何慧洁, 王慧敏, 刘静怡, 等. 机械通气对危重型新型冠状病毒肺炎合并ARDS患者的救治作用 [J]. *中国中西医结合急救杂志*, 2020, 27 (5): 532-535. DOI: 10.3969/j.issn.1008-9691.2020.05.005.
- He HJ, Wang HM, Liu JY, et al. Rescue and therapeutic effect of mechanical ventilation on patients with severe coronavirus disease 2019 complicated with acute respiratory distress syndrome [J]. *Chin J TCM WM Crit Care*, 2020, 27 (5): 532-535. DOI: 10.3969/j.issn.1008-9691.2020.05.005.
- [19] Longhini F, Pisani L, Lungu R, et al. High-flow oxygen therapy after noninvasive ventilation interruption in patients recovering from hypercapnic acute respiratory failure: a physiological crossover trial [J]. *Crit Care Med*, 2019, 47 (6): e506-e511. DOI: 10.1097/CCM.0000000000003740.
- [20] Bellani G, Laffey JG, Pham T, et al. Epidemiology, patterns of care, and mortality for patients with acute respiratory distress syndrome in intensive care units in 50 countries [J]. *JAMA*, 2016, 315 (8): 788-800. DOI: 10.1001/jama.2016.0291.
- [21] Antonelli M, Conti G, Esquinas A, et al. A multiple-center survey on the use in clinical practice of noninvasive ventilation as a first-line intervention for acute respiratory distress syndrome [J]. *Crit Care Med*, 2007, 35 (1): 18-25. DOI: 10.1097/01.CCM.0000251821.44259.F3.
- [22] Patel BK, Wolfe KS, Pohlman AS, et al. Effect of noninvasive ventilation delivered by helmet vs face mask on the rate of endotracheal intubation in patients with acute respiratory distress syndrome: a randomized clinical trial [J]. *JAMA*, 2016, 315 (22): 2435-2441. DOI: 10.1001/jama.2016.6338.
- [23] Ríos FG, Estenssoro E, Villarejo F, et al. Lung function and organ dysfunctions in 178 patients requiring mechanical ventilation during the 2009 influenza A (H1N1) pandemic [J]. *Crit Care*, 2011, 15 (4): R201. DOI: 10.1186/cc10369.
- [24] Almekhlafi GA, Albarrak MM, Mandourah Y, et al. Presentation and outcome of Middle East respiratory syndrome in Saudi intensive care unit patients [J]. *Crit Care*, 2016, 20 (1): 123. DOI: 10.1186/s13054-016-1303-8.
- [25] Stéphan F, Barrucand B, Petit P, et al. High-flow nasal oxygen vs noninvasive positive airway pressure in hypoxemic patients after cardiothoracic surgery: a randomized clinical trial [J]. *JAMA*, 2015, 313 (23): 2331-2339. DOI: 10.1001/jama.2015.5213.
- [26] Coudroy R, Jamet A, Petua P, et al. High-flow nasal cannula oxygen therapy versus noninvasive ventilation in immunocompromised patients with acute respiratory failure: an observational cohort study [J]. *Ann Intensive Care*, 2016, 6 (1): 45. DOI: 10.1186/s13613-016-0151-7.
- [27] Frat JP, Ragot S, Coudroy R, et al. Predictors of intubation in patients with acute hypoxemic respiratory failure treated with a noninvasive oxygenation strategy [J]. *Crit Care Med*, 2018, 46 (2): 208-215. DOI: 10.1097/CCM.0000000000002818.
- [28] Rello J, Pérez M, Roca O, et al. High-flow nasal therapy in adults with severe acute respiratory infection: a cohort study in patients with 2009 influenza A/H1N1v [J]. *J Crit Care*, 2012, 27 (5): 434-439. DOI: 10.1016/j.jcrc.2012.04.006.
- [29] Hernandez-Romieu AC, Adelman MW, Hockstein MA, et al. Timing of intubation and mortality among critically ill coronavirus disease 2019 patients: a single-center cohort study [J]. *Crit Care Med*, 2020, 48 (11): e1045-e1053. DOI: 10.1097/CCM.0000000000004600.
- [30] Agarwal R, Aggarwal AN, Gupta D. Role of noninvasive ventilation in acute lung injury/acute respiratory distress syndrome: a proportion meta-analysis [J]. *Respir Care*, 2010, 55 (12): 1653-1660.
- [31] Burns GP, Lane ND, Tedd HM, et al. Improved survival following ward-based non-invasive pressure support for severe hypoxia in a cohort of frail patients with COVID-19: retrospective analysis from a UK teaching hospital [J]. *BMJ Open Respir Res*, 2020, 7 (1): e000621. DOI: 10.1136/bmjresp-2020-000621.
- [32] Hu HD, Ma FL, Wei X, et al. Coronavirus fulminant myocarditis treated with glucocorticoid and human immunoglobulin [J]. *Eur Heart J*, 2021, 42 (2): 206. DOI: 10.1093/eurheartj/ehaa190.
- [33] Chen C, Zhou YW, Wang DW. SARS-CoV-2: a potential novel etiology of fulminant myocarditis [J]. *Herz*, 2020, 45 (3): 230-232. DOI: 10.1007/s00059-020-04909-z.
- [34] Zeng JH, Liu YX, Yuan J, et al. First case of COVID-19 complicated with fulminant myocarditis: a case report and insights [J]. *Infection*, 2020, 48 (5): 773-777. DOI: 10.1007/s15010-020-01424-5.
- [35] 胡凯, 李卜军. 重型和危重型新型冠状病毒肺炎患者死亡危险因素 Logistic 回归分析及其预测价值 [J]. *中华危重病急救医学*, 2020, 32 (5): 544-547. DOI: 10.3760/cma.j.cn121430-20200507-00364.
- Hu K, Li BJ. Logistic regression analysis of death risk factors of patients with severe and critical coronavirus disease 2019 and their predictive value [J]. *Chin Crit Care Med*, 2020, 32 (5): 544-547. DOI: 10.3760/cma.j.cn121430-20200507-00364.
- [36] Esteban A, Frutos-Vivar F, Ferguson ND, et al. Noninvasive positive-pressure ventilation for respiratory failure after extubation [J]. *N Engl J Med*, 2004, 350 (24): 2452-2460. DOI: 10.1056/NEJMoa032736.
- [37] Carrillo A, Gonzalez-Diaz G, Ferrer M, et al. Non-invasive ventilation in community-acquired pneumonia and severe acute respiratory failure [J]. *Intensive Care Med*, 2012, 38 (3): 458-466. DOI: 10.1007/s00134-012-2475-6.
- [38] Bourke SC, Piraino T, Pisani L, et al. Beyond the guidelines for non-invasive ventilation in acute respiratory failure: implications for practice [J]. *Lancet Respir Med*, 2018, 6 (12): 935-947. DOI: 10.1016/S2213-2600(18)30388-6.
- [39] Fisher KA, Mazon KM, Goff S, et al. Successful use of noninvasive ventilation in chronic obstructive pulmonary disease. How do high-performing hospitals do it? [J]. *Ann Am Thorac Soc*, 2017, 14 (11): 1674-1681. DOI: 10.1513/AnnalsATS.201612-1005OC.
- [40] Bravata DM, Perkins AJ, Myers LJ, et al. Association of intensive care unit patient load and demand with mortality rates in us department of veterans affairs hospitals during the COVID-19 pandemic [J]. *JAMA Netw Open*, 2021, 4 (1): e2034266. DOI: 10.1001/jamanetworkopen.2020.34266.