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ORIGINAL ARTICLE

Management of patients with severe acute respiratory failure due to SARS-CoV-2 pneumonia with noninvasive ventilatory support outside Intensive Care Unit

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ABSTRACT

BACKGROUND: COVID-19 has high mortality rate mainly stemming from acute respiratory distress leading to respiratory failure (ARF). Aim of the study was to evaluate the management of severe ARF due to COVID-19 pneumonia using noninvasive ventilatory support (NIVS), studying safety and effectiveness of NIVS.

METHODS: This is a retrospective, multicenter study. Primary outcomes were NIVS failure with intubation rate and hospital mortality. Secondary outcomes were hospital stay and factors related to NIVS failure and mortality. These outcomes were compared with patients intubated and admitted to ICU.

RESULTS: One hundred sixty-two patients were hospitalized because of severe respiratory failure (PaO_2/FiO_2 ratio <250). One hundred thirty-eight patients were admitted to Respiratory Intermediate Care Unit (RICU) for a NIVS trial. One hundred patients were treated successfully with NIVS (74.5%); 38 failed NIVS trial (27.5%). In-hospital mortality was 23.18% in RICU group and 30.55% in ICU group. Patients with NIVS failure were older, had a lower number of lymphocytes, a higher IL-6, lower PaO_2, PaC O_2, PaO_2/FiO_2 ratio, higher respiratory rate (RR) and heart rate at admission and lower PaO2, and PaO_2/FiO_2 ratio and higher RR after 1-6 hours. Multivariate analysis identified higher age, C-reactive protein as well as RR after 1-6 hours and PaO_2/FiO_2 ratio after 1-6 hours as an independent predictor mortality.

CONCLUSIONS: NIVS is a safe and effective strategy in the treatment of severe ARF due to COVID-19 related pneumonia, that reduces mortality and length of hospital stay in the carefully selected patients.

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KEY WORDS: COVID-19; Respiratory insufficiency; Hospital mortality.

The use and the choice of a ventilatory support for acute respiratory failure (ARF) due to SARS-Coronavirus 2 (SARS-CoV-2) pneumonia has been widely debated. Due to a lack of established treatment protocols against the virus' severest manifestations, clinicians need to rely

on the experience gained in similar conditions.[1-3] In the first weeks of pandemic most patients were managed in intensive care units (ICUs) with invasive ventilation (IMV) as for other similar forms of ARF. After an initial period of viral replication with fever and non-specific symptoms, typically five to ten days, a subsequent phase may follow in which excessive inflammatory response produces diffuse alveolar damage, edema, endothelial damage with vascular thrombosis. In Coronavirus disease 2019 (COVID-19) ARF most often occurs within ten to fifteen days of initial viral invasion and may develop in just a few hours. Early treatment may limit an exaggerated inflammatory response. The careful selection of patients to treat with IMV as well as the very recent recognition that noninvasive ventilatory support (NIVS) (*e.g.* high flow nasal cannula [HFNC], continuous positive airway pressure [CPAP], noninvasive ventilation [NIV]) has an important role in therapy. A recent article demonstrated NIVS to be useful in patients with COVID in ARF cases.[2] Patients with ARF as a consequence of SARS-CoV-2 typically show hypoxia, generally associated with respiratory alkalosis, a decreased paO_2/FiO_2 ratio values, and an increase in arterial alveolar O_2-gradient (A-a DO_2). The mechanisms of hypoxia are principally linked to alteration in the ventilation/perfusion ratio with variable vascular shunt effect in the alveolar areas which are frequently excluded from ventilation.[3]

Very recently, the concept of phenotypes of hospitalized COVID patients have suggested as guides to treatment.[4, 5] Both protocols may be termed types of presentation. Both are based on computerized tomography (CT). Each cautions the physician to be aware of thrombosis. Gattinoni *et al*. have hypothesized that COVID-19 patients presents with the two different phenotypes: 1) type L (low) presents with "diminished lung elastance, low ventilation to perfusion ratio,l ow lung weight and low lung recruitability (the amount of nonaerated lung tissue is low);" 2) type H (high) is characterized by "high pulmonary elastance, high right to left shunt, high lung weight, and high lung recruitability."[4]

In the L presentation, CT of the chest demonstrates modest localized sub-pleural interstitial edema (ground glass) which triggered by the virus itself. Type L may deteriorate into type H. Here there are bilateral lung infiltrates and acute respiratory distress syndrome (ARDS).[4, 5]

An early study from Wuhan including 18 patients with COVID-19 admitted to ICU suggested a significantly poor pulmonary recruitability and compromised hemodynamic perfusion due to disrupted vaso-regulation caused by vascular insult. Thus, the common approach of applying high levels of positive expiratory pressure (PEEP) may lead worse outcomes.[6]

In our study we aimed to evaluate the safety and the effectiveness of NIVS in patients with severe ARF (PaO_2/FiO_2 less than 250) due to SARS-CoV-2 pneumonia.

Materials and methods

This retrospective observational study was conducted in respiratory intermediate care units (RICUs) of Hospital of Santander, Spain, and Don Gnocchi Foundation Milan, Italy, and COVID Intensive Care Unit (ICU). The Local Institutional Review Boards approved this study as minimal-risk research using data collected for routine clinical practice. Due to the nature of retrospective review, the Boards waived the need for informed consent. Between March 14, 2020 and May 20, 2020, 162 consecutive patients who required hospital admission with confirmed acute respiratory syndrome SARS-CoV-2 infection *via* positive polymerase chain reaction test of nasopharyngeal swab sample and who showed severe ARF (fraction of inspired oxygen [FiO_2], arterial partial pressure of oxygen [PaO_2] PaO_2/FiO_2 ratio less than 250) due to pneumonia were included in the study.

Exclusion criteria included requirement for rapid endotracheal intubation for cardiopulmonary resuscitation, respiratory arrest, severe hemodynamic instability, severe encephalopathy and more than two new extrapulmonary organ failures. Figure 1 shows study patients flow chart. Patients' degree of severity and organ failure were estimated with Simplified Acute Physiology Score (SAPS) II. Twenty-four of 162 patients required immediate intubation and were admitted directly to ICU.

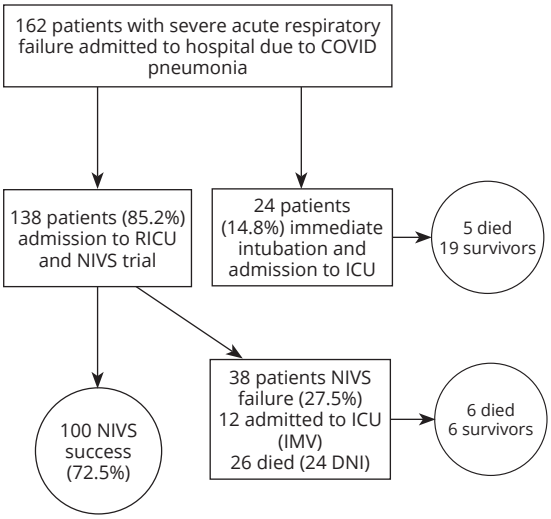

Figure 1.—Study flowchart.
RICU: Respiratory intermediate care unit; ICU: Intensive care unit; NIVS: Non-invasive ventilatory support; IMV: Invasive mechanical ventilation (intubation); DNI: Do not intubate order; COVID: Corona virus disease.

The remaining 138 patients underwent a NIVS trial to avoid endotracheal intubation. All centers followed a clinical flow chart as described in previous studies on pandemics.[7] Predetermined major criteria for admission to ICU after NIVS included failure to maintain PaO_2/FiO_2<100 or development of conditions which require urgent airway protection such as coma, failure to manage copious tracheal secretions, any hemodynamic instability, inability to tolerate the interface and/or inability to resolve dyspnea.[7] A further criterion added to clinical flow was the distinction between L-type and H-type using CT evaluation.[4, 5] A good interface fitting was guaranteed (24 hours/day) with timed checks by health-care workers. Moreover, every medical or health-care worker staff member wore a single-layer respiratory PPE with gown, gloves, visor and fit-tested FFP3 mask.[8] NIV was delivered using either ICU ventilators or dedicated NIV platforms ventilators with double limb circuits. The most commonly used ventilation modes were pressure support ventilation (PSV), bi-level positive airway pressure (Bi-PAP) and less often pressure control ventilation (PCV). When using the helmet, the titration of the ventilation was based upon what described by Vargas *et al*.[9] with an increase of 50% in both pressure support (PS)and positive end-expiratory pressure (PEEP) provided at the highest pressurization rate. The health care team consisted of infectious disease physicians, pulmonologists, experts on mechanical ventilation, nurses, physiotherapists. A pulmonologist with particular expertise in mechanical ventilation was present in the units 12 hours per day and on call the other 12 hours. The nurse patient ratio was 1:3 to 1:4. It was possible to switch from NIVS to IMV at any moment. The therapeutic protocol included:

- antiviral drugs;
- hydroxychloroquine 200 mg bid for seven days;[10]
- corticosteroid therapy (dexamethasone 6 mg/day or methylprednisolone 40-120 mg/day);[11, 12]
- empiric antibiotics directed at community acquired pneumonia (*e.g.* ceftriaxone 2 gr iv/day plus azithromycin 500 mg iv/day);
- standard prophylactic coagulation with low molecular weight heparin. Therapeutic anticoagulation was used in documented thromboembolism;[10]
- tocilizumab 4-8 mg/kg in two administration in case of elevate interleukin-6 levels (IL-6).[11-13]

The information for all patients, including demographic data, medical comorbidities, clinical features, laboratory parameters, mode of respiratory support, level of PEEP, arterial blood gases analysis (ABG), PaO_2/FiO_2 ratio, the choice of interface were recorded. The number of patients who had died, had been discharged, length of hospital stay, hospital and 28-day mortality were also noted. At admission patients had continuous monitoring of electrocardiogram, arterial oxygen saturation, blood pressure, respiratory rate (RR), and heart rate (HR). The following parameters were recorded: age, sex, comorbidities, arterial blood gases (ABG), ventilation mode, and settings. ABG were withdrawn at a fixed interval after 1 -6 hours, 24 hours from the beginning of NIVS and afterward at the discretion of the attending physician.[7] The patients were divided in two groups: respiratory intensive care unit (RICU) admission and intensive care unit (ICU) admission; results were compared between the two groups.

Primary endpoints were NIVS failure and intubation rate, hospital mortality and 28-day mortality. Secondary outcomes were: hospital stay and factors related to NIVS failure and mortality.

Statistical analysis

Continuous data were expressed as means and standard deviation (SD) and categorical variables as proportions. Logistic regression was used to evaluate univariate associations. Variable with P values <0.05 were included in the multivariate logistic regression mode with a conditional stepwise model to correct for colinearity. Adjusted odds ratio and 95% confidence intervals were associated with hospital mortality. A P value <0.05 was considered significant. Data analysis was made with SPSS statistics version 25 software (IBM; Armonk, NY, USA).

Results

One hundred sixty-two patients (92 males and 56 females) 66.87±16.6 years old were admitted to hospital because of severe ARF due to COVID-19 pneumonia. 24 patients (14.8%) underwent immediate intubation and admission to ICU. The primary reason for immediate intubation and ICU admission was cardio-respiratory arrest (6 patients), septic or cardiac shock (4 patients), rapid worsening respiratory failure (7 patients) and multiorgan failure (MOF) (6 patients). One hundred thirty-eight patients were admitted to RICU for a NIVS trial. Among the patients treated with NIVS 28 were treated with HFNC, 59 with CPAP delivered with oro-nasal mask or helmet (32 and 17 respectively), 51 with NIV delivered with oro-nasal or total face mask or helmet (22, 18 and 11 respectively).

Setting parameters according to respiratory support were the follows: HFNC flow 50.0±15.0, CPAP–PEEP 10.3±2.7 cm H_2O and NIV–PEEP 9.5±3.1 with pressure support (PS) 14.6±7.4 cm H_2O.

Patients admitted to ICU were significantly younger than those admitted to RICU (62.06±13.2 *versus* 70.98±14.75) and had more severe illness (SAPS II and CURB-65). Moreover, they had more severe respiratory impairment than those admitted to RICU (PaO_2 and PaO_2/FiO_2). Six of 162 patients (6.2%) had a Do Not Intubate orders (DNI) and were admitted to RICU. Baseline characteristics of patients at admission are summarized in Table I. Most patients were male (64.4%). Hypertension, diabetes, obesity and cardiovascular disorders were the most frequent comorbidities. Obesity (BMI>30) were the most represented comorbidity (56.9%).

One hundred patients were treated successfully with NIVS (72.5%); 38 failed NIVS trial (27.5%). The primary reason for NIVS failure was worsening of respiratory failure and ARDS (eight patients), multi-organ failure (eight patients), severe cardiac injury (two patients), septic shock (two patients), and severe renal failure (one patient). Among 38 NIVS failure twelve were intubated and admitted to ICU, 6 were DNI

TABLE I.—*Baseline characteristics of patients at admission.*

Variable	RICU (138 pts)	ICU (24 pts)	P value
Sex (M%)	62.3%	66.6%	0.07
Age (years)	70.98±14.75	62.06±13.21	0.002
SAPS II score	26±8	34±6	0.01
CURB 65 score	1±1	2±1	0.07
Past medical history			
Cardiovascular disorders	7 (5.0%)	4 (16.6%)	0.01
Hypertension	34 (24.65%)	7 (29.1%)	0.27
Diabetes	16 (11.5%)	6 (25.0%)	0.03
Respiratory disorders	4 (2.8%)	5 (20.8%)	0.001
Malignancy	4 (2.8%)	1 (4.1%)	0.12
Chronic kidney diseases	3 (2,1%)	1 (4.1%)	0.44
Neurological disorders	4 (2.8%)	2 (8.3%)	0.04
Obesity	71 (51.45)	15 (62.5%)	0.06
Immunosuppression treatment	2 (1.44%)	1 (4.1%)	0.04

(To be continued)

TABLE I.—*Baseline characteristics of patients at admission (continues).*

Variable	RICU (138 pts)	ICU (24 pts)	P value
Clinical findings			
Fever	134 (97.15%)	23 (95.83%)	0.66
Cough	67 (54.03%)	16 (66.6%)	0.03
Dyspnea	128 (92.7%)	22 (91.66%)	0.59
Chest pain	12 (8.69%)	3 (12.5%)	0.04
Syncope	2 (1.44)	3 (12.5)	0.003
Headache	13 (9.42%)	3 (12.5%)	0.07
Myalgia	104 (75.36%)	17 (70.83%)	0.09
Diarrhea	10 (7.24%)	3 (12.5%)	0.05
Time from symptoms onset to hospital admission (days)	7.90±3.89	8.53±3.94	0.14
Time from symptoms onset to ventilatory support (days)	9.14±4.18	9.72±3.85	0.19
Laboratory values			
Red blood cells 10^6 u/L	4.20±0.752	4.21±0.721	0.26
White blood cells u/L	7783±4809	8399±4788	0.67
Lymphocytes cells u/L	927.07±588.12	695.00±528.22	0.02
Platelet 10^3 u/L	237.45±111.49	254.19±131.08	0.56
C-reactive protein mg/dL	9.64±9.34	11.99±10.99	0.11
Pro-calcitonin mcg/L	7.56±58.03	2,31±9.69	0.59
Ferritin mcg/L	851.3±1160.8	715.64±802.4	0.34
Interleukin 6 pg/mL	13,81±31.23	32.76±57.77	0.009
APTT ratio	33.88±4.88	35.72±6.78	0.13
PT %	92.22±17.74	90.33±18.49	0.44
AT III %	94.39±35,33	94.28±15.23	0.46
Fibrinogen mg/dL	441.57±152.97	515.17±211.52	0.02
D-Dimer ng/ml	4.71±8.03	3.86±7.41	0.25
Creatinine kinase U/L	213.14±705.56	163.28±141.98	0.18
AST U/L	62.84±48.3	52.92±34.48	0.34
ALT U/L	46.49±39.29	63.03±60.25	0.22
Lipase U/L	75.54±60.07	52.22±46.90	0.23
BNP ng/L	145.95±74.44	254.44±74.33	0.02
Troponin ng/L	118.78±60.9	89.50±28.83	0.09
Creatinine mg/dL	1.088±0.94	1.209±1.21	0.31
Sodium mmol/L	135.2±4.3	136.8±3.7	0.24
Potassium mmol/L	3.99±0.77	4.01±0.63	0.19
Calcium mg/dL	7.8±1.1	7.7±1.4	0.33
Glucose mg/dL	114.6±12.8	123.4±23.6	0.10
LDH U/L	396.73±349.97	357.58±139.87	0.14
Radiological findings			
Monolateral pneumonia	5 (3.62%)	1 (4.16%)	0.08
Bilateral pneumonia	133 (96.3%)	22 (91.6%)	0.21
Type L phenotype	128 (92.8%)	10 (41.75)	0.003
Type H phenotype	10 (7.2%)	14 (58.3%)	0.001
Respiratory parameters			
Respiratory rate	31.92±1.94	33.14±2.30	0.02
Heart rate	95.78±4.79	105.86±8.42	0.01
paO_2 mmHg	42.78±7.12	34.47±7.50	0.01
$paCO_2$ mmHg	37.38±9.18	44.61±24.51	0.09
pH	7.46±0.53	7.41±0.51	0.04
$satO_{2\%}$	85.78±4.79	83.28±3.23	0.06
PaO_2/FiO_2	203.49±35.77	161.19±34.77	0.001
$AaDO_2$ mmHg	60.7±10.2	61.5±9.99	0.10
Lactate mmol/L	2.1±1.0	3.4±1.3	0.05

Variables are expressed as numerical and percentage values for dichotomic variables and mean and standard deviation (SD) for continuous variables.
RICU: respiratory intermediate care unit; ICU: Intensive Care Unit; SAPS II: simplified acute physiology score; CURB 65: CURB-65 score for pneumonia severity; APTT: activated partial thromboplastin time; PT: prothrombin time; AT: antithrombin III; AST: aspartate aminotransferase, ALT: alanine aminotransferase; BNP: brain-type natriuretic peptide; LDH: lactate dehydrogenase; paO_2: arterial partial pressure of oxygen; $paCO_2$: arterial partial pressure of carbon dioxide; $satO_2$: arterial oxygen saturation; paO_2/FiO_2: arterial partial pressure of oxygen fraction concentration of oxygen in inspired air ratio; $AaDO_2$: alveolar-arterial oxygen gradient; RR: respiratory rate (breaths/min); HR: heart rate (beats/min).

order and 20 died without an expressed written DNI order and were not intubated after an evaluation of a multidisciplinary team in which included pulmonologists, intensivists, and anesthesiologists along with experts in medical ethics were involved.[14]

In hospital mortality was 23.18% in RICU group and 30.55% in ICU group, but mortality in patients admitted immediately to ICU was 20.83%. Overall, 28-day mortality was 30.70%; 90-day mortality was 33.2%.

Patients with NIVS failure were older than those in whom NIVS succeeded. A lower number of lymphocytes, a higher IL-6 ($P<0.001$) as well as lower PaO_2, $PaCO_2$, PaO_2/FiO_2 ratio higher respiratory rate (RR) and heart rate (HR) at admission ($P<0.001$ and 0.002). Furthermore, NIVS failure were associated with lower PaO_2 and PaO_2/FiO_2 ratio and higher RR after 1-6 hours. Variables associated to NIVS failure are reported in Table II.

Hospital survivors was younger, had a shorter hospital stay and lower D-Dimer, C-reactive protein, troponin, ferritin, LDH, CPK at admission as well as lower SAPS-II on initial evaluation. Moreover, they presented with higher PaO_2 and PaO_2/FiO_2 at admission as well as a higher PaO_2/FiO_2 ratio and lower RR after 1-6 h (Table III). Multivariate analysis identified higher age, C-reactive protein, RR after 1-6 hours and PaO_2/FiO_2 ratio after 1-6 hours as an independent predictor of hospital mortality (Table IV).

Discussion

This study demonstrated that NIVS was effective in reducing intubation rate and mortality. To our knowledge only a few previous studies have explored the use of NIVS in severe ARF due to COVID -19 related pneumonia outside ICU.[15-17]

The first study of NIV in a cohort of 1305 patients together with mortality predictors. NIV was used in 21.1% of patients and IMV in 24.9%. Age greater than 60 years and increasing number of comorbidities were independent predictors of in-hospital mortality.[15] In another study reported a little cohort (fifteen patients) treated with NIV (associated with prone position) in mild to moderate ARDS. All patients showed a reduction of RR and improvement PaO_2/FiO_2 ratio. Among them, thirteen improved, one was intubated, and one died.[16] The latter is an observational study including 670 patients with ARF due COVID-19 related pneumonia. The authors noted an intubation rate of 27% and 30-day mortality of 26.9%. Mortality rate increased with age and comorbidities.[17] Two further studies included 38 and 30 patients were carried out in two respiratory and emergency wards. The authors have reported a hospital mortality 50% and 26.7% respectively. Mortality was associated with higher PEEP.[18, 19] Our data are in accord with those reported previously: we have observed NIVS failure was 27.5% and hospital mortality 23.18%. It is interesting to observe that these results did

TABLE II.—*Variable associated with failure of NIVS.*

Variable	Survivors (106 pts)	Not survivors (32 pts)	P value
Age	62.1±13.2	71.6±14.8	0.001
Lymphocytes	695.0±528.9	953.5±599.2	0.03
IL-6 pg/mL	28.1±22.26	63.9±50.78	0.001
PaO_2 at admission	43.4±6.7	36.6±7.5	0.001
$PaCO_2$ at admission	44.6±4.5	37.0±7.8	0.001
paO_2/FiO_2 ratio at admission	174.2±36.2	161.1±34.7	0.0001
RR at admission	31.7±1.8	33.1±2.3	0.02
HR at admission	100.7±7.7	109.00±4.1	0.007
PaO_2 after 1-6 h	106.0±20.4	89.7±7.4	0.001
PaO_2/FiO_2 after 1-6 h	251.2±61.3	186.7±43.5	0.002
RR after 1-6 h	26.3±4.0	31.4±3.6	0.019

Variables are expressed as mean and standard deviation (SD).
NIVS: noninvasive ventilatory support; IL -6: interleukin 6; paO_2: arterial partial pressure of oxygen; $paCO_2$: arterial partial pressure of carbon dioxide; $paO_2/_{FiO2}$: arterial partial pressure of oxygen/fraction concentration of oxygen in inspired air ratio; RR: respiratory rate (breaths/min); HR: heart rate (beats/min).

TABLE III.—*Variables associated with mortality.*

Variable	Survivors (125 pts)	Not survivors (37 pts)	P value
Age	66.0±10.0	69.1±3.8	0.0001
D-dimer mg/L	4.5±2.6	7.8±2.5	0.001
Lymphocytes cells/mm^3	658.6±502.7	967.9±448.3	0.002
CRP mg/dL	8.7±8.5	13.5±6.3	0.002
Ferritin mcg/L	631.89±343.7	1297.7±589.6	0.016
Troponin ng/L	34.7±19.4	308.12±91.0	0.004
LDH U/L	312.±142.3	576.6±188.5	0.001
BNP pg/mL	88.6±78.18	646.1±370.8	0.001
CK U/L	148.6±119.8	1136.5±408.5	0.001
PaO_2 at admission	42.2±3.6	38.0±8.2	0.001
PaO_2/FiO_2 ratio at admission	200.9±37.3	179.2±11.5	0.001
PaO_2 /FiO_2 after 1-6 h	200.9±37.3	179.21±25.4	0.001
RR after 1-6 hours	24.4±3.6	32.0±3.2	0.001
Hospital stay	17.0±4.7	22.5±4.7	0.002

Variables are expressed as mean and standard deviation (SD). Statistical significance was set for P<0.05.
CRP: C-reactive protein; LDH: lactate dehydrogenase; BNP: brain-type natriuretic peptide;
CK creatine phosphokinase; PaO_2: arterial partial pressure of oxygen; PaO_2/FiO_2: arterial partial pressure of oxygen/fraction concentration of oxygen in inspired air ratio; RR: respiratory rate (breaths/min).

TABLE IV.—*Multivariate analysis of variables independently associated with hospital mortality.*

Variable	OR	95% CI	P value
Age	1.09	1.04-1.14	0.0001
CRP	1.08	1.01-1.15	0.016
PaO_2/FiO_2 after 1-6 h	0.97	0.96-0.98	0.02
RR after 1-6 h	1.39	1.04-1.85	0.0001

CRP: C reactive protein; paO_2/FiO_2: arterial partial pressure of oxygen/fraction concentration of oxygen in inspired air ratio; RR: respiratory rate (breaths/min).

not differ from some important and larger studies made in ICU (from 21% to 24.5%).[20, 21] Also, predictors of failure were similar to previous studies.[15, 20-23] Protection of health care worker should be another significant aspect in COVID pandemic management. For this reason, personal protective equipment and negative pressure rooms or at least rooms with natural ventilation should be employed.[19] Following all the suggested precautions and protection some studies reported an infection rate tested *via* pharyngeal swab or serology in health workers about 10%.[19, 24] In our units a protocol similar to the protocol in Wuhan study was implemented.[25] FFP3 masks available for all operators. Furthermore, aerosol mode was not used to administer respiratory drugs. By following strictly, a developed protocol for COVID-19 intensive care only seven of 112 health workers (6.25%) developed COVID-19, but only two required hospital admission. A final consideration regards the criteria suggested to evaluate the plausible phase of the disease: we have used it and took into consideration the different location and instrumentation in the therapy of ARF.[26] In patients with CT and or lung ultrasound patterns suggesting a L-phenotype a NIVS trial with low-moderate PEEP and low tidal volumes to redistribute pulmonary blood flow from damaged to normal lung areas was started. When a H-phenotype (ARDS-like pattern) was diagnosed predominant high PEEP and prone position was employed; these patients were most often treated in the ICU.[4, 5, 26] These radiological criteria should be used in concert with the epidemiological, clinical and laboratory severity of patient's illness to determine the better ventilation choice for that patient.[27-31] In a recently published study Demoule *et al*. studied 379 COVID-19 patients admitted to four ICUs; these investigators found a significant reduction of IMV and a similar 28-day mortality compared to patients intubated from the beginning. The authors explain this observation: SARS-CoV-2 infection does not coincide with the typical courses or features of ARDS.[32]

Limitations of the study

This study has some limitations. The retrospective design does not permit definitive conclusions about the effectiveness of NIVS. Second,

the decision to start NIVS modes was left to the attending physician and not always discussed by a multidisciplinary team. The critical nature of the situation did not always permit a shared decision. Change in treatment strategy was always an option.

Conclusions

In summary, severe and critical COVID-19 patients are a challenge for intensivists. From the beginning of pandemic patients with severe ARF were treated with NIVS. Our experience with severe COVID-19 admitted to our RICUs can help and encourage clinicians to consider the possibility of using NIVS in selected patients. This option has shown a favorable rate of success manifested by an apparent improvement in mortality and reduced the length of hospital stay in the carefully selected patient.

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