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LETTER

Djamel Mokart
Cyrille Geay
Laurent Chow-Chine
Jean-Paul Brun
Marion Faucher
Jean-Louis Blache
Magali Bisbal
Antoine Sannini

High-flow oxygen therapy in cancer patients with acute respiratory failure

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Dear Editor,

Acute respiratory failure is a dramatic event and remains a major cause of ICU admission in cancer patients [1]. It has been recently shown that high-flow oxygen therapy through a nasal cannula in association with noninvasive ventilation (HFNC–NIV) during acute respiratory failure is associated with high mortality in unselected patients with hypoxemic acute respiratory failure (FLORALI study) [2]. We retrospectively analyzed 178 cancer patients admitted to the ICU for severe acute respiratory failure (O_2 delivery >9 L/min). We computed a propensity score to predict HFNC–NIV treatment based on specific characteristics at ICU admission. The primary outcome was all-causes mortality at day 28; secondary outcomes included the number of ventilator-free days at day 28 and long-term mortality. The study was approved by our institutional review board. For the initial population ($n = 178$), pulmonary infection (any pathogen) was present in 116 patients (65 %). At ICU admission the median SAPS II was 47 (IQR 38–57), SOFA score 6 (4–9), and PaO_2/FiO_2 ratio 123 (87–158). A total of 150 patients (84 %) were treated with NIV, 84 (47 %) with HFNC, and 94 (53 %) with standard oxygen. Among these patients, 76 (43 %) were treated with HFNC–NIV, 74 (42 %) with standard O_2–NIV, 8 (5 %) with standard O_2 alone, and 20 (11 %) with HFNC alone. As compared to the others patients, HFNC–NIV patients presented a lower day-28 mortality rate, 37 % ($n = 28$) vs 52 % ($n = 53$), $p = 0.045$; a longer time from ICU admission to intubation 34 h (18–72) vs 16 h (7–45), $p = 0.01$; and a higher but not significant number of ventilator-free days, 24 (2–28) vs 8 (1–28), $p = 0.06$. A total of 138 patients were included in the propensity analysis [Table 1, supplementary material (SM) 1]. Day-28 mortality was 36 % in HFNC–NIV patients and 54 % in other patients (Table 1, $p = 0.027$). After adjustment for the propensity score, HFNC–NIV was independently associated with improved survival (SM 2). Ventilator-free days and day-90 mortality were significantly in favor of HFNC–NIV patients (Table 1, SM 3). Intubation rates at day 28 were similar in the two group of patients: 48 % (HFNC–NIV patients vs 52 % (other patients), $p = 0.277$ (Table 1).

In contrast to recent data [2], we describe significant improvement of day-28 mortality in cancer patients with acute respiratory failure treated with HFNC–NIV as compared with other patients. Although our patients presented with severe acute respiratory failure, mortality rate was particularly encouraging in the HFNC–NIV group, whereas intubation rate and delay of intubation were comparable to those of the FLORALI study [2]. However from our results, the risk of delayed intubation in the HFNC–NIV group has not been clearly evaluated. In our ICU, NIV protocol is strictly standardized; however, at the bedside, controlling for expiratory tidal volume is not easily feasible continuously. In contrast, our NIV presets were always 0.5 h/session (up to 1 h) and four sessions/24 h (up to 6) [3]. NIV treatment in cancer patients is under investigation and needs to be evaluated in the context of the recent survival improvement of these patients [4]. Acute respiratory failure in cancer patients is frequently associated with severe mucositis, tracheal bleeding, and/or alveolar hemorrhage, and under these conditions pulmonary sepsis may be exacerbated by bloody thick secretions. HFNC may prevent from secretions retention, atelectasis [5], and need for invasive mechanical ventilation [2]. Accordingly, in our study HFNC–NIV was associated with more ventilator-free days and less septic shock occurrence. Interestingly, the day-28 mortality rate of patients never treated with NIV was 7/15 (47 %) vs 55/123 (45 %) for others patients, $p = 0.89$. Regarding patients never treated with HFNC, the day-28 mortality rate was 36/63 (57 %) vs 26/75 (35 %) for HFNC patients, $p = 0.008$. These findings strongly suggest that the use of NIV was not associated with adverse effects, whereas the use of HFNC was associated with survival. These preliminary results suggest that a trial of HFNC in cancer patients with acute respiratory failure is warranted.

Table 1 Characteristics of the matched patients

	HFNC–NIV ($n = 69$)	Others ($n = 69$)	p
Age, years[a]	56 (46–66)	59 (47–66)	0.931
Female gender[a]	28 (41)	29 (42)	0.695
Charlson co-morbidity index[a]	5 (4–7)	5 (3–7)	1
Underlying malignancy[a]			
Acute leukemia	17 (25)	20 (29)	0.847
Lymphoma	17 (25)	16 (23)	1
Myeloma	2 (3)	1 (1)	0.571
CML, CLL	6 (9)	7 (10)	0.594
Others hematology diseases	4 (6)	6 (9)	0.739
Solid tumors[a]	27 (39)	26 (38)	1
Metastasis	24 (35)	20 (29)	0.435
Allogeneic HSCT[a]	11 (16)	13 (19)	0.655
Autologous HSCT[a]	9 (13)	6 (9)	0.618
ARF etiology[a]			
Pulmonary sepsis	45 (65)	45 (65)	1
Malignant involvement	13 (19)	6 (9)	0.083
Pulmonary embolism	3 (4)	3 (4)	1
Mechanical participation	4 (6)	10 (14)	0.121
Others	11 (16)	17 (25)	0.396
At ICU admission			
SAPS II[a]	47 (37–55)	48 (38–59)	0.577
SOFA score[a]	6 (4–8)	6 (4–9)	0.737
PaO_2/FiO_2 ratio	128 (89–154)	116 (85–163)	0.948
Sepsis	58 (84)	55 (80)	0.638
Microbiologically documented sepsis	38 (55)	31 (45)	0.292
Bacteria	26 (38)	23 (33)	0.602
Fungi	14 (20)	16 (23)	0.670
Virus	12 (17)	9 (13)	0.638
Neutropenia[a]	24 (35)	24 (35)	0.853
Neutropenia recovery	5 (7)	3 (4)	0.739
During ICU stay			
Vasopressors	44 (64)	42 (61)	0.857
Evolution toward septic shock	10 (15)	24 (35)	**0.012**
RRT	10 (15)	15 (22)	0.257
Standard oxygen	–	63 (91)	–
Standard oxygen alone	–	9 (13)	
HFNC	69 (100)	6 (9) (HFNC alone)	–
NIV	69 (100)	54 (78)	0.049
Days with NIV	4 (3–5)	4 (4–6)	0.881
Intubation rate at day 28	33 (48)	36 (52)	0.277
With PaO_2/FiO_2 <200 at admission	29/63 (46)	29/57 (51)	0.396
PaO_2/FiO_2 ratio (intubation)	89 (58–147)	88 (74–121)	0.364
Time from admission to intubation (h)	30 (17–52)	13 (6–47)	0.251
With PaO_2/FiO_2 <200 at admission	27 (16–52)	12 (6–47)	0.593
Invasive ventilator-free days at day 28 ψ	19 (1.4)	14 (1.6)	**0.019**
Outcome			
Treatment limitations in ICU	18 (26)	21 (30)	0.435
ICU length of stay (days)	9 (5–15)	6 (3–12)	0.082
Hospital length of stay (days)	16 (9–32)	12 (5–19)	**0.016**
Mortality of ventilated patients at day 28	17/33 (52)	26/36 (72)	0.076
Mortality at day 28	25 (36)	37 (54)	**0.027**

Data are expressed as number (%), median (IQR), or mean (SEM) ψ

Statistics: logistic regression with a random effect or a Cox random effect model (length of stay)

Bold values indicate significant results, $p < 0.005$

CML chronic myeloid leukemia, *CLL* chronic lymphocytic leukemia, *ARF* acute respiratory failure, *HSCT* hematopoietic stem cell transplantation, *SAPS II* simplified acute physiology score II, *SOFA* sequential organ failure assessment score, *RRT* renal replacement therapy, *HFNC* high-flow oxygen therapy through a nasal cannula, *NIV* noninvasive ventilation, *ICU* intensive care unit

[a] Parameters used for computing the propensity score. A 1:1 matching algorithm without replacement was used within a given range of 0.20 standard deviations of the logit of the estimated propensity score

Compliance with ethical standards

Conflicts of interest The authors declare no conflict of interest.

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D. Mokart (✉) · C. Geay · L. Chow-Chine · J.-P. Brun · M. Faucher · J.-L. Blache · M. Bisbal · A. Sannini
Polyvalent Intensive Care Unit, Department of Anesthesiology and Critical Care Medicine, Institut Paoli Calmettes, 232 Boulevard Sainte Marguerite, 13009 Marseille Cedex 09, France
e-mail: mokartd@ipc.unicancer.fr
Tel.: +33491223521
URL: http://www.grrroh.com

D. Mokart
GRRR-OH (Groupe de Recherche en Réanimation Respiratoire en Onco-Hématologique), Paris, France