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Original Contribution

Arterial pH selectively predicts critical care needs in emergency department obese patients with acute dyspnea: A prospective comparative study

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ABSTRACT

Introduction: Obese patients with acute dyspnea may be prone to misorientation from the emergency department (ED), due to impaired gas exchange evaluation and altered basal respiratory profiles. This study aims to evaluate the prognostic value of arterial blood pH in obese ED patients with acute dyspnea in comparison to non-obese counterparts.
Methods: Single-center observational study of a cohort of 400 consecutive ED patients with acute dyspnea. The primary endpoint was a composite of Intensive Care Unit admission (with critical care needs) or in ED mortality. Predictors of the primary endpoint were assessed using multivariable logistic regression and ROC curve analysis, in obese (BMI ≥ 30 $kg \cdot m^{-2}$) and non-obese patients.
Results: 252 patients who had arterial blood gas testing were analyzed including 76 (30%) obese comparable to non-obese in terms of clinical history. 51 patients were admitted to ICU and 2 deceased before admission (20 obese (26%) vs 33 non-obese (19%); $p = 0.17$). Factors associated with ICU admission were arterial blood pH (pH < 7.36 vs pH ≥ 7.36) and gender. In multivariate models adjusted for risk factors, pH remained the sole independent predictor in obese patients, with no predictive value in non-obese patients (ROC AUC: 0.74, 95% CI [0.60; 0.87], optimal threshold for pH: 7.36, odds ratio: 10.5 [95% CI 3.18; 34.68]).
Conclusion: Arterial blood pH may selectively predict critical care needs in ED obese patients with acute dyspnea, in comparison to non-obese. A falsely reassuring pH < 7.36 should be regarded as a marker of severity when assessing acute dyspnea in obese ED patients.

1. Introduction

1.1. Background

As the prevalence of obesity raises in industrialized countries, the number of obese patients requiring emergency care increases and may represent up to a third of the total number of ED admissions. Obesity is characterized by dysfunctions of the respiratory system, due to decreased expiratory flows and lung volumes – particularly the functional residual capacity – as a consequence of a reduced thoraco-abdominal compliance [1,2].

Acute dyspnea is a common chief complaint among patients who present to the emergency department (ED), with numerous underlying causes to consider. It has been shown to be associated with the highest in-hospital mortality in the unselected acute population of ED patients [3].

Evaluation of acute dyspnea is a challenge, and even more in the obese patients. Clinical examination is often poorly contributive. Alteration of gas exchange is difficult to interpret, given altered baseline levels of $PaCO_2$ and PaO_2, especially in the ED where patient's baseline values are seldom available. Higher respiratory rates, normal to slightly reduced hypoxemia and less frequently hypercapnia tend to be baseline features of obese patients' respiratory profiles [4].

Thus anticipating the course and differentiating the severity of acute respiratory dysfunction in obese patients is critical. Early identification of patients at risk of deterioration is essential, notably for patients requiring critical care as early orientation to ICU has been shown to be associated with reduced mortality [5,6].

Multiple strategies, most based on clinical score or blood markers, have been explored for risk assessment in patients with acute dyspnea in the ED [7-22]. Only 2 studies evaluated the prognostic value of readily

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available blood gas parameters in unselected dyspneic ED patients. Buri et al. showed that arterial blood pH is predictive of admission to the ICU as well as predictive of 30 days and 12 months mortality, while Lund et al. demonstrated that total carbon dioxide predicted readmission to the ED or death at 12 months [18,23].

The principal aim of this study is to assess the prognostic value of arterial blood gas analysis in a cohort of unselected ED patients presenting with dyspnea of any cause, comparing obese and non-obese patients.

2. Methods

2.1. Study design and setting

This was a prospective single center observational, prognostic study conducted from May 2013 to May 2014 in a French urban University Hospital ED (Montpellier University hospital) with a yearly census of 56,000 adult patients.

Patients were consecutive patients from a prospective cohort of patients presenting with acute dyspnea and who had an ABG analysis as part of the ED standard management. Obese (BMI ≥ 30 $kg \cdot m^{-2}$) and non-obese (BMI < 30 $kg \cdot m^{-2}$) patients were compared. The primary endpoint was a composite of admission to intensive care unit (ICU) or ED mortality before transfer to the ICU.

Study was conducted in accordance with the Declaration of Helsinki and with the STROBE statement for observational studies [24] and TRIPOD statement for reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis.

Study approval was deemed unnecessary by the ethics committee due to the observational nature of the study (Comité de Protection des Personnes Sud Méditterranée IV, ref #02014-09-05). Clinical Trials registration: NCT03239730.

2.2. Study population

Adult patients who were admitted to the ED with acute dyspnea formed the study cohort. Eligible patients were patients who had an ABG analysis in the ED. Non-inclusion criteria were 1. treatment limitation decisions made by the medical team against ICU admission, including severe cognitive impairment ($n = 19$) or palliative care ($n = 12$), and 2. life-threatening conditions requiring immediate transfer to ICU at ED admission (patients with shock requiring vasopressors, patients with altered mental status (Glasgow ≤ 10), patients in need for immediate mechanical ventilation requiring immediate transfer to ICU ($n = 1$ hemorrhagic shock) (Fig. 1).

2.3. Outcome measure

The main outcome was determined a priori and defined as admission to the ICU with receipt of ICU level of care or in ED mortality. Admission to the ICU at our institution is based on current guidelines [25], and in agreement with the attending ICU physician. Patients with acute respiratory failure are transferred to the ICU if they require continuous ventilation support (either invasive mechanical ventilation or non-invasive ventilation), or present with hemodynamic instability requiring continuous vasoactive drug infusions or with other organ failure.

2.4. Data collection

Data was recorded using a standardized form: patient's characteristics, medical history, vital signs at ED admission (blood pressure, heart rate, pulse oximetry and respiratory rate), arterial blood gas parameters (partial pressure of arterial oxygen (PaO_2), partial pressure of arterial

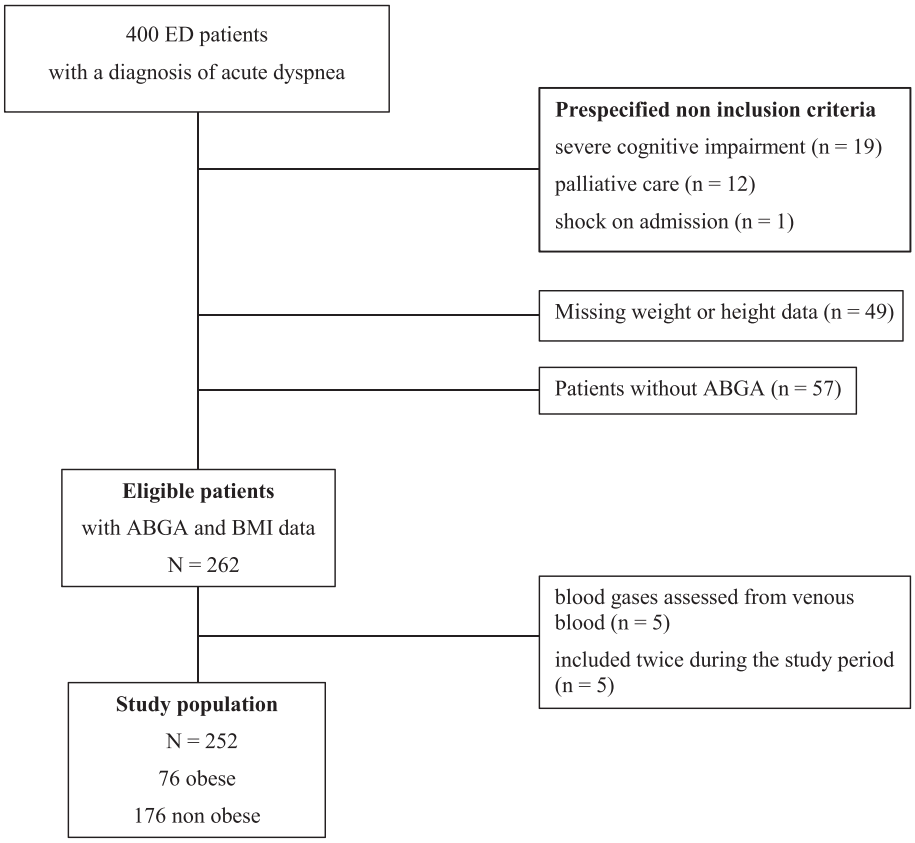

Fig. 1. Flowchart of study patients.

carbon dioxide ($PaCO_2$), pH, bicarbonate concentration (HCO_3^-) and base excess), laboratory analysis results (complete blood count, C-reactive protein, high-sensitivity troponin and NT proBNP plasma levels) and ED discharge diagnosis, orientation (ICU with receipt of intensive care level of care, ward, discharge).

Obesity was defined as BMI ≥ 30 kg/m^2 according to the World Health Organization definition.

Organ failure was defined as the presence of either of the following criteria: systolic blood pressure < 90 mm Hg, Glasgow coma scale < 10, platelets < 100 G/L, blood creatinine >177 μmol/L according to the 2012 Surviving Sepsis Campaign international guidelines for management of severe sepsis and septic shock [26].

2.5. Arterial blood gas analysis

The decision to perform ABG analyses was at the discretion of the attending ED physician. ABG analyses were carried out according to clinical routine testing in our biochemistry laboratory. Blood (1 mL) was sampled by radial artery puncture and collected into heparinized syringes. ABG analyses were performed using the Omni-S™ COBAS B221 (Roche Diagnostics France France) system at the central biochemistry laboratory. Normal ranges were: pH = 7.35–7.45; $PaCO_2$ = 35–45 mm Hg; O_2 = 78–98 mm Hg; HCO_3^- = 22–26 mmol/L; base excess = −2 to +2 mmol/L. Acidosis was defined as pH ≤ 7.34.

2.6. Statistical analysis

Descriptive statistics were performed using frequencies for qualitative variables, mean and standard deviation (SD), or median and interquartile range (IQR) for continuous variables according to their normal distribution.

Unadjusted associations between patient characteristics were examined using Student or Mann-Whitney *U* test for quantitative variables and Chi-square test or Fisher's exact test for categorical variables, as appropriate. Obese patients were compared to non-obese patients.

2.7. Receiver operating characteristics curves (ROC)

ROC curves and their area under the curve (AUC) were built to estimate the accuracy of arterial blood gas parameters in predicting ICU admission and their optimal thresholds. Optimal cut-off points were determined using the best combined sensitivity and specificity. AUC, sensitivity and specificity were calculated along with 95% confidence interval (95% CI).

2.8. Multivariate regression analysis

Associations between ICU admission and blood gas parameters, patient characteristics and other clinically relevant factors previously shown to be associated with ICU admission (adjustment factors) were assessed by univariate logistic regression. Possible collinearity between predictive variables were searched. Factors entered in the univariate models were: pH (as continuous variable and as pH < 7.36 vs pH ≥ 7.36), base excess (for every 1 mmol/L increase), $PaCO_2$ (for every 10 mm Hg increase), lactate (for every 1 mmol/L increase), age (for every 1 year increase), gender (male vs female), history of pulmonary disease, history of COPD, history of pulmonary disease other than COPD, history of chronic kidney disease, history of chronic heart failure and organ failure.

Factors retained in the univariate analysis ($p < 0.20$) were subsequently added to the multivariable logistic regression model to identify independent predictors. Factors were selected using stepwise selection with 0.20/0.05 entry/exit criteria and verified using backward selection.

Results were expressed as adjusted odds ratios, calculated along with their 95% confidence intervals. The Hosmer Lemeshow test was performed to assess the goodness-of-fit of the logistic model.

We did not include lactate levels in multivariate analysis due to the low number of lactate results. Base excess was not included in the multivariate analysis due to multicollinearity with $PaCO_2$.

Hypothesis testing was performed using two-tailed statistical tests with a significance level of 0.05. Statistical analysis was performed by RS at the statistics department of our University Hospital, using SAS version 9.2 (SAS Institute Inc.; Cary, NC).

3. Results

3.1. Characteristics of study subjects

During the study period, 400 patients presented with acute dyspnea, including 57 patients (14.3%) for whom blood gas analysis was deemed unnecessary by the attending ED physician (Supplementary data).

The study population comprised 252 patients out of the 342 ED patients who had blood gas testing including 76 (30%) obese patients (BMI ≥ 30) (Fig. 1).

Obese and non-obese patients were comparable in age, sex, smoking habits, history of respiratory disease, chronic kidney disease or heart failure. Obese patients were more likely to present with a history of diabetes and high blood pressure, to have an ED discharge diagnosis of acute exacerbation of COPD/asthma, and a lower mean pH, higher BE and $PaCO_2$ (Table 1).

3.2. Main results

3.2.1. ICU admission (with need for ICU level of care)

Twenty three out of 252 (9%) patients were directly discharged home, 176 (70%) were hospitalized.

Fifty three (21%) patients were admitted to the ICU, including two patients deceased in the ED before transfer (one from acute heart failure and one from pulmonary embolism. Of these, 31 (58%) patients were male and 22 female (41%), and 20 (38%) were obese (Table 2).

All 53 patients had respiratory failure. Six patients had additional kidney failure, 2 had additional hemodynamic failure and 2 had all three organ failures.

All patients admitted to the ICU received ICU level of care: 3 received invasive ventilation, 39 received non-invasive ventilation, 4 received high flow oxygen therapy (≥6 L/min), 4 received vasoactive medication and 2 underwent hemodialysis.

Variables associated with a higher rate of admission to the ICU were: a history of respiratory disease ($p = 0.024$) and acidosis ($p = 0.009$). Obesity was not associated with a higher rate of admission to the ICU ($p = 0.1762$) (Table 2).

3.2.2. Independent predictors of ICU admission (with need for ICU level of care) in the whole study population

In ROC analysis, pH moderately discriminated between patients for ICU admission. ROC AUC was 0.55 [95%CI: 0.46–0.64]. At the optimal cut point of pH < 7.36, sensitivity was 43% [95% CI: 30–57] and specificity was 76% (95% CI: 70–82).

In multivariable analysis, pH < 7.36 and male sex were two independent predictors of ICU admission, after adjusting for BE, $PaCO_2$, history of pulmonary disease and organ failure. There was no adjustment with lactate due to missing data (data only available in 89 patients). Odds ratio for ICU admission are shown in Tables 3 and 4.

3.2.3. Independent predictors of ICU admission (with need for ICU level of care) in obese patients

In ROC analysis, pH moderately discriminated between patients admitted to the ICU and those who were not. ROC AUC was 0.76 [95%CI:

Table 1
Characteristics of the study population according to obesity status.

Variable	Non-obese ($N = 176$)	Obese ($N = 76$)	p
Age, year	74 (58.5–84.5)	66.5 (58–80)	0.1
Male sex	85 (48.3)	34 (44.7)	0.6
Smoking status			
Smokers	51 (29)	25 (33)	0.65
Non smokers	71 (40.3)	25 (33)	
Never smoked	35 (19.9)	15 (19.7)	
Unknown	19 (10.8)	11 (14.5)	
Medical history			
Ischemic cardiopathy	42 (23.9)	23 (30.3)	0.29
Diabetes	38 (21.6)	38 (50)	6.10^{-6}
Arterial hypertension	91 (51.7)	55 (72.4)	0.002
Respiratory disease			
– BPCO	40 (22.7)	18 (23.7)	0.65
– Other than BPCO	25 (14.2)	14 (18.4)	
Chronic kidney disease	20 (11.4)	12 (15.8)	0.33
Chronic heart failure	25 (14.2)	14 (18.4)	0.83
Clinical parameters			
Temperature	37 (37–38)	37 (36.8–37.3)	0.44
Systolic blood pressure	141 (122–163)	141 (126–170)	0.56
Diastolic blood pressure	76 (68–86)	79 (67–90)	0.49
Heart rate (beats/min))	96 (80–100)	95 (76–105)	0.34
Respiration rate (breath/min)	28 (23–35)	28 (24–35)	0.74
Oxygen saturation (%)	92 (88–96)	93 (88–96)	0.93
Arterial blood gas parameters			
pH	7.40 (7.36–7.44)	7.38 (7.36–7.42)	0.031
$PaCO_2$ (mm Hg)	39 (34–44)	42 (35–60)	0.01
Base excess (mmol/L)	−0.45 (−2.30–1.25)	0.15 (−1.65–3.60)	0.02
Acidosis (pH < 7.35)	34 (19.3)	19 (25)	0.31
Lactate (mmol/L)	1.45 (1–2.45)	2 (1.40–3.30)	0.08
Other variables of interest			
Prehospital oxygenotherapy	117 (66.5)	49 (64.5)	0.76
Organ dysfunction	29 (17.4)	8 (10.7)	0.18
ED discharge diagnosis			
Decompensated heart failure	50 (28.4)	24 (31.6)	0.61
COPD exacerbation asthma	37 (21)	27 (35.5)	0.02
Pneumonia	80 (45.5)	33 (43.4)	0.77
Pulmonary embolism	12 (6.8)	5 (6.6)	0.94

Data are shown for all 252 patients of the study cohort including 76 obese (BMI ≥ 30) and 176 non-obese patients, except for lactate results only available in $n = 89$ patients including 25 obese patients.
Data are reported as numbers and (percentages) or median with (interquartile range). Respiratory disease other than COPD includes cystic fibrosis, lung cancer and severe restrictive syndrome related to lateral amyotrophic sclerosis. COPD: chronic obstructive pulmonary disease. BMI: Body Mass Index.

Table 2
Characteristics of the study population according to their orientation following ED management.

Variable	Other orientation ($n = 199$)	ICU admission ($n = 53$)	p
Age	72 (59–83)	73 (58–80)	0.76
Female sex	111 (55.8)	22 (41.51)	0.06
Obesity (BMI ≥ 30)	56 (28.1)	20 (37.7)	0.18
Medical history			
Respiratory disease			0.024
– COPD	41 (20.6)	17 (32.1)	
– Other than COPD	27 (13.6)	12 (22.6)	
Chronic kidney disease	23 (11.6)	9 (17)	0.29
Heart failure	37 (18.6)	14 (26.4)	0.21
Blood gas parameters			
pH	7.40 (7.37–7.44)	7.41 (7.34–7.43)	0.23
PaO_2			
$PaCO_2$			
Base excess (mmol/L)	−0.3 (−2.3–1.6)	−0.2 (−2–3.6)	0.24
Acidosis (pH < 7.35)	35 (17.8)	18 (34)	0.009
Lactate (mmol/L)	2.20 (1.40–3.40)		

Data are reported as numbers and (percentages) or median and (interquartile range).
Data are shown for all 252 patients of the study population including 53 patients transferred to ICU and 199 patients who were either discharged home or hospitalized from ED. Lactate testing was only performed in n = 89 patients including 24 transferred to ICU.
Respiratory disease other than COPD includes cystic fibrosis, lung cancer and severe restrictive syndrome related to lateral amyotrophic sclerosis.
Organ dysfunction: systolic blood pressure < 90 mm Hg, Glasgow coma scale < 10, platelets < 100 G/L and blood creatinine > 177 μmol/L.
BMI: Body Mass Index; COPD: chronic obstructive pulmonary disease.

0.62–0.89]. At the optimal cut point of pH < 7.36, sensitivity was 75% (95%CI: 56–94) and specificity was 80% (95%CI: 70–91).

In multivariate analysis, pH < 7.36 was the sole factor associated with ICU admission, after adjusting for $PaCO_2$, history of pulmonary disease, history of COPD and organ failure (Tables 3–4).

ROC AUC for the predictive model was 0.74 [95%CI: 0.60–0.87).

3.2.4. Independent predictors of ICU admission (with need for ICU level of care) in non-obese patients

In ROC analysis, pH did not discriminate between patients admitted to the ICU and those who were not. ROC AUC was 0.56 [95%CI: 0.45–0.67]. At the optimal cut point of pH < 7.41, sensitivity was 67% (95%CI: 51–83) and specificity was 51% (95%CI: 43–59).

In multivariate analysis, sex was the sole independent predictor of ICU admission after adjusting for pH, history of pulmonary disease, including history of COPD, history of heart failure and organ dysfunction (Table 3-4).

4. Limitations

This was a single center study of observational design.

However our data might be transposable to other ED centers as dyspneic patients who met the study endpoint all benefited from ICU level of care.

We focused on unselected patients presenting with acute dyspnea of all causes with ABG results obtained at ED admission, thus reflecting real life conditions at ED admission.

The decision to perform ABG testing was at the discretion of the attending emergency physician which is a major limit of this observational study. We cannot rule out a selection bias toward more severe patients. However 78% of our acutely dyspneic patients had ABG analysis, and 30-day mortality (8%) and hospital admission were similar to that reported in studies of comparable size [20,23].

Table 3
Factors associated with ICU admission in univariate analysis.

	OR for ICU admission	p
Study population		
pH < 7.36 vs pH ≥ 7.36	2.41 (1.23–4.74)	0.011
$PaCO_2$	1.33 (1.08–1.66)	0.009
History of COPD	2.26 (1.11–4.62)	0.025
History of pulmonary disease other than COPD*	2.43 (1.08–5.44)	0.031
Obese patients		
pH < 7.36 vs pH ≥ 7.36	10.50 (3.18–34.68)	0.0001
$PaCO_2$	1.61 (1.15–2.26)	0.006
Non-obese patients		
Male gender vs female	3.01 (1.33–6.77)	0.008
History of cardiac failure	2.48 (1.06–5.78)	0.036

Results of univariate analysis in the whole study population and in obese and non-obese patient subgroups. Only factors significantly associated with ICU admission are shown. Odds ratio (OR) are reported with 95% CI. pH ≥ 7.36 and female gender are used as reference.
BMI: Body Mass Index; COPD: chronic obstructive pulmonary disease.
* Respiratory disease other than COPD includes cystic fibrosis, lung cancer and severe restrictive syndrome related to lateral amyotrophic sclerosis.

Table 4
Factors independently predictive of ICU admission in multivariate analysis.

Predictive factors	OR for ICU admission	*p*
Study population		
pH < 7.36 vs pH ≥ 7.36	2.87 (1.41–5.81)	0.004
Male vs female	2.13 (1.12–4.06)	0.021
Obese patients		
pH < 7.36 vs pH ≥ 7.36	10.50 (3.18–34.68)	0.0001
Non-obese patients		
Male vs female	3.01 (1.33–6.77)	0.008

Results of the multivariate logistic regression analysis in the whole study population and in obese and non-obese patient subgroups. Only significant factors are shown, after adjusting for $PaCO_2$, history of pulmonary disease, history of COPD and organ failure. Odds ratio (OR) are reported with 95% CI. pH ≥ 7.36 and female gender used as reference. COPD: chronic obstructive pulmonary disease.

We could not include lactate values in multivariate logistic regression due to missing data, which may be a confounding factor even though patients with shock at admission were excluded from the study population.

5. Discussion

This is to our knowledge the first study exploring the prognostic value of blood gas parameters in the specific population of obese patients presenting with acute dyspnea to the ED, compared to non-obese. We demonstrate that arterial blood pH is the sole independent predictor of need for ICU care in obese patients, after adjustment for $PaCO_2$, history of pulmonary disease, history of COPD and organ failure. Arterial blood pH did not predict ICU admission in non-obese patients.

Our findings obtained from consecutive patients with acute dyspnea of whom 30% were obese confirm those of Burri et al. [23]. However we further show that pH predicts need for ICU care specifically for obese patients in comparison to non-obese patients, with a threshold value of pH within the lower limit of normal range as compared to that obtained in Burri's study (7.36 versus 7.39).

Compared to Burri's study, ABG testing was more frequent in our dyspneic patients, with 80% (versus 50%) of our patients tested, while both cohorts were comparable in terms of outcome. The rate of hospitalization (70% vs 87%), ICU admission (21% vs 17%) and 30 day-mortality were similar in both studies (8.5% vs 10.2%). They also compared well with a more recent prospective study also evaluating unselected acutely dyspneic patients presenting to a Norwegian ED [20].

Obese and non-obese patients were similar in terms of personal history, except for diabetes and arterial hypertension. Obese patients showed significantly higher $PaCO_2$ values, as well as significantly lower pH values, than non-obese patients at ED admission. The lower pH threshold for ICU admission in obese patients in our study may be a consequence of the impact of obesity on alveolar ventilation. One possible explanation could be that respiratory comorbidities such as syndrome of sleep apnea, COPD or OHS remain largely undiagnosed among obese patients. Indeed, a final diagnosis of COPD exacerbation was more frequent in the obese patient group (35% vs 21% for COPD/asthma) even though the percentage of patients with a history of COPD was not different between obese and non-obese patients (23%).

In obese patients, regulatory systems may be less efficient at compensating the further increase in $PaCO_2$ associated with acute episodes of dyspnea. Hence a slight change of pH may indicate a later and more severe stage of the pathological process in this population.

pH is a readily available parameter, obtained from standard arterial blood gas analysis at ED presentation. It could be used as a decision-making tool to aid clinical assessment and guide early orientation of ED obese patients with acute dyspnea.

6. Conclusion

Our study shows that arterial blood pH obtained at ED admission may predict needs for ICU care specifically for obese patients presenting with acute dyspnea, while it has no predictive value in non-obese patients. Our study also suggests that a falsely reassuring pH < 7.36 should be regarded as a marker of severity in obese patients presenting with acute dyspnea to the ED.

Our findings are the results of an observational study, in which ABG testing was at the discretion of the attending ED physician. Our findings could aid early detection of dyspnea severity and guide the management and orientation in these patients, providing validation in further studies.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ajem.2018.04.059.

Data show characteristics of all eligible patients from the study cohort including 57 patients who did not have arterial blood gas testing as part of ED management and were thus excluded from the study population.

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Meetings

Study was presented at the French society for Emergency Medicine conference (SFMU 2015), on June 11th 2015 in Paris, France, and at the French society for anesthesia and critical care conference (SFAR 2015) on September 19th, 2015 in Paris, France.

Authors' contributions

MS conceived the study. All authors participated in the study design, development of study protocol and data collection. RS performed the statistical analysis. VG, SL and MS drafted the manuscript, and all authors contributed substantially to its revision. MS takes responsibility for the paper as a whole. All authors read and approved the final manuscript.

Consent for publication

Not applicable (no individual data).

Availability of data and material

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The author(s) declare(s) that they have no competing interests.

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