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Incidence and risk factors of weaning-induced pulmonary oedema: results from a multicentre, observational study

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Abstract

Background During the weaning process, the transition from positive to negative pressure ventilation may induce cardiac dysfunction, which may lead to pulmonary oedema. The incidence of weaning-induced pulmonary oedema (WIPO) is poorly documented and shows huge variations. Our study aims to investigate the incidence and risk factors for WIPO during weaning from mechanical ventilation in general critically ill patients.

Methods This multicentre study was conducted in France, Italy, and India. Adult critically ill patients receiving invasive ventilation were included once a spontaneous breathing trial (SBT) was performed. The SBT technique could be either T-piece or pressure support mode with (PSV-PEEP) or without positive end expiratory pressure (PEEP) (PSV-ZEEP). A consensual diagnosis of WIPO was made a posteriori by five experts who analysed changes observed during the SBT that were retrospectively recorded.

Results From July 2019 to February 2021, 634 SBTs were performed in 500 patients from 13 ICUs. Weaning success occurred in 417 patients (66%) and weaning failure in 217 (34%). Weaning was short in 414 (83%) of SBTs, difficult in 47 (9%) SBTs, and prolonged in 39 (8%) SBTs. WIPO was diagnosed in 79 (12%) cases, which accounted for 36% of the 217 weaning failures. WIPO occurred in 54/358 (15%) of T-piece SBT, in 7/84 (8%) of PSV-PEEP SBT ($p = 0.072$ *vs.* T-piece), and in 18/192 (9%) of PSV-ZEEP SBT ($p = 0.002$ *vs.* T-piece). In multilevel logistic regression analysis including 202 weaning failures from 149 different patients, COPD, and previous cardiomyopathy were identified as independent risk factors associated with WIPO.

Conclusion In general ICU patients, WIPO accounts for 36% of weaning failure cases. Previous heart disease and COPD are two independent risk factors for developing WIPO during the weaning process.

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Keywords Weaning, Spontaneous breathing trial, Heart–lung interaction, COPD

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Introduction

Mechanically ventilated patients who fail being separated from the ventilator may experience prolonged ventilation, prolonged stay in the intensive care unit (ICU) [1, 2], and poor prognosis [1, 3]. Among the causes of weaning failure, the transition from positive to negative pressure ventilation may induce cardiac dysfunction, which may lead to pulmonary oedema (weaning-induced pulmonary oedema, WIPO) [4, 5]. WIPO was first described in patients with chronic obstructive pulmonary disease (COPD) and concomitant cardiovascular disease [6].

Although it is likely one of the main reasons for weaning failure [6], the true incidence of WIPO is poorly documented. Only few studies reported WIPO [7–16], and showed huge variations of its incidence varying from 14% [15] to 100% [14] of the weaning failure cases (Supplemental Table S1). However, these studies included small numbers of patients [7, 11] and/or a specific population who had already failed one or more spontaneous breathing trials (SBTs) [14, 17, 18]. Liu et al. reported that WIPO occurred in 59% of weaning failures [18], but this was in a monocentric study including rather severe critically ill patients who had already failed one or more SBT.

The risk factors for WIPO are neither well determined. Knowing these risk factors is important to optimize and personalize patients' management [19]. The above-cited study showed that patients who suffered from chronic obstructive pulmonary disease (COPD), previous cardiomyopathy and obesity were more likely to experience WIPO [18], but again, it was performed in a specific population.

The primary objective of the current study was to determine the incidence of WIPO in a mixed population of critically ill patients. The secondary objectives were to determine the characteristics of patients who experienced WIPO, and the risk factors of WIPO.

Patients and methods

This multicentre, observational study was performed in ICUs of 13 tertiary hospitals (ClinicalTrials.gov NCT05318261) (Supplemental Table S2). It was approved by the ethics committee of the French Intensive Care Society (2017-A00392-51) and of each centre (Supplemental Table S2). Informed consent was obtained from each patient or from the patient's legally authorized representative if the patient was unable to provide consent. Alternatively, deferred informed consent was obtained from patients.

Study population and spontaneous breathing trial

Adult critically ill patients receiving invasive ventilation were included once the attending physicians decided to perform an SBT. We excluded patient on extracorporeal membrane oxygenation, patients with a decision to withdraw life-sustaining therapy, including do-not-reintubate orders, and patients with tracheostomy. Patients could be included several times.

The decision to perform an SBT was taken by clinicians in charge. The SBT could be performed either by disconnecting the tracheal tube from the ventilator and connecting it to an oxygen source via a "T-piece" or by using the pressure support mode with (PSV-PEEP) or without PEEP (PSV-ZEEP) [20]. The criteria for performing an SBT and the decision to systematically start non-invasive ventilation after extubation were not protocolised.

The SBT failure was defined as the occurrence of one of the following: dyspnoea (respiratory rate ≥ 35 breaths/min or increase ≥ 50%) or oxygen desaturation with pulsed saturation (SpO_2) < 90% despite increase of the oxygen flow to 6L/min or higher (T-piece) or increased FiO_2 to 50% or higher (PSV-PEEP or PSV-ZEEP) or systolic hypertension ≥ 200 mmHg or hypercapnia with arterial carbon dioxide partial pressure ≥ 42 mmHg. If failure occurred during the SBT performed on a T-piece, patients were reconnected to the ventilator. Extubation failure was defined as the need for unplanned treatment with non-invasive ventilation after extubation or reintubation in the 48 h following extubation [21, 22]. We defined weaning failure as an SBT failure or an extubation failure [20].

We classified patients into three groups according to the WIND definitions [3]: "short" weaning (successful weaning or death ≤ 24 h after the first SBT), "difficult" weaning (successful weaning or death more than 1 day but less than 7 days following the first SBT) and "prolonged" weaning (successful weaning or death at least 7 days following the first SBT).

Recorded variables

The collected demographic data included past cardiovascular and respiratory medical history, simplified acute physiology score (SAPS) II and sequential organ failure score (SOFA), presence of acute respiratory distress syndrome (ARDS) [23], the main reason for intubation, the duration and mode of mechanical ventilation before the SBT and the use of vasopressors.

Previous cardiomyopathy was defined as dilated and/or hypertrophic cardiomyopathy, focal or diffuse hypokinetic cardiomyopathy, significant valvular disease, defined as aortic or mitral regurgitation of grade ≥ 2, mild or severe aortic, mitral stenosis and atrial fibrillation before the ICU admission. The result of the last echocardiography examination performed before SBT was recorded. The patient's weight was measured at ICU admission and then every day. Fluid balance over the last 24 h before the SBT was calculated. The diagnosis of

COPD was established on the following criteria: chronic and progressive dyspnoea, cough, and sputum production [24]. These symptoms were retrospectively collected from the patient's previous medical reports or from the interview of the patient or his/her relatives.

A posteriori, we collected the following data, recorded before and after the SBT as a part of current care: haemodynamic (heart rate, arterial pressure) and respiratory variables (dyspnoea, respiratory rate, SpO_2, diaphoresis), arterial blood gas analysis if available, E and A waves of the mitral flow, and e' wave of the external mitral annulus at echocardiography if available, the number of B-lines in the four anterior quadrants of the thorax at lung ultrasound [25] if available, cardiac index, extravascular lung water and global end-diastolic volume if measured by transpulmonary thermodilution, an electrocardiogram and results of biological tests including troponin Ic, B-type natriuretic peptide or NT-pro- B-type natriuretic peptide, haemoglobin, and plasma protein concentration, if available.

Diagnosis of WIPO

A consensual diagnosis of WIPO was made a posteriori on anonymised data by five experts (JLT, NA, DO, TP, XM) who were not involved in inclusion [18]. They particularly took into account the following changes observed during the SBT: changes in heart rate and/or arterial pressure, increases in respiratory rate and effort, development of crackles on auscultation, hypoxemia as indicated by pulse oximetry and/or blood gas analysis, increase of the E/A and E/e' ratios at echocardiography, increase in the number of B-lines at lung ultrasound, in extravascular lung water, in haemoglobin and plasma protein concentration indicating haemoconcentration [17], in B-type natriuretic peptide or NT-pro- B-type natriuretic peptide, in troponin Ic dosage, and changes in the electrocardiogram. Experts were not informed of the patient's history, the success or failure of the SBT, and the modalities of the SBT. Consensus on the presence or absence of WIPO was considered reached if at least four of the five experts agreed on the diagnosis after discussion. If this was not the case, a discussion was organised again. If consensus, defined in the same way, was still not reached, the diagnosis was considered inconclusive.

Statistical analysis

Categorical and quantitative data are presented as frequency (percentage) and mean ± standard deviation or median (interquartile range), as appropriate. Statistical analysis was performed using parametric (Fischer's exact test and paired Student's t-test) or non-parametric tests (Mann–Whitney and Wilcoxon tests), as appropriate. Proportions were compared with Pearson's Chi-squared or Fischer's exact tests.

We performed bivariate analysis to identify variables associated with the occurrence of weaning failure and of WIPO. Variables found to be significantly associated with the occurrence of weaning failure and of WIPO with a p-value < 0.20 at univariate analysis and clinically relevant were introduced into a multivariable logistic regression model. Considering the hierarchical nature of this study, we performed mixed effect logistic regression analyses [26, 27] to identify covariates associated with weaning failure and those associated with the occurrence of WIPO. This two-level random intercept binary logistic regressions comprised a first level including SBT related variables (e.g., time from intubation to SBT, type of SBT) and a second level including patients related variables (e.g., comorbidities, severity at admission). We selected variables a priori based on their clinical relevance or their expected association with the outcomes of interest and we tested in the model additional variables found associated with the outcomes of interest in bivariate analysis. Results are shown as odds ratios (ORs) with 95% confidence interval (95% CI). The prediction model was established based on the logistic model. The power of predictive model was represented by the area under the receiver operating characteristic curve (AUROC) for each model using the Delong method. We planned to include 500 patients. No assumptions were made for missing data. Statistical analyses were done with MedCalc 19.2.1 software (MedCalc Software Ltd, Ostend, Belgium) and R (version 4.1.0). All p values were two-sided, and values less than 0.05 were deemed statistically significant.

Results

Population

From July 2019 to February 2021, 13 centres including six medical ICUs, six mixed ICUs, and one surgical ICU participated in the study. In total, 634 SBTs were performed in 500 patients. Their baseline characteristics are presented in Table 1. The main indication for intubation was acute respiratory failure or shock or sepsis.

Result of SBTs

T-piece was used in 257 (51%) patients, PSV-PEEP in 80 (16%) patients, and PSV-ZEEP in 163 (33%) patients. The median duration of SBT was 60 (40–66) mins and 84 (13%) SBTs were performed while patients were receiving vasopressors (0.10 (0.04–0.28) µg/kg/min). Among the 634 SBTs performed, 417 (66%) succeeded, and 217 (34%) failed, including 31 (14%) which occurred in patients who were initially extubated and reintubated within 48 h. Weaning was "short" in 414

Table 1 Comparison of patient characteristics between the succeeded and at least once failed spontaneous breathing trials

Variables	Weaning success N = 343	Weaning failure N = 157	*p*-value
Age (y.o.)	66 (54–75)	64 (55–74)	0.607
Male (n, %)	234 (68)	87 (55)	**0.006**
SOFA score	8 (5–11)	8 (6–11)	0.621
SAPS II score	52 ± 18	54 ± 19	0.259
BMI (kg/m^2)	26.2 (22.3–31.0)	26.2 (23.0–31.1)	0.706
Duration of MV before the SBT (mins)	4 (2–9)	6 (3–10)	**0.001**
Duration of weaning procedures (mins)	60 (45–70)	60 (32–65)	**0.003**
Indication of intubation (n, %)			
ARF/shock			
Acute respiratory failure/sepsis/shock	134 (39)	92 (59)	**< 0.001**
Septic shock without pneumonia	40 (12)	16 (10)	0.628
Other shock types (hypovolaemic, cardiogenic, and vasoplegia non-septic)	14 (4)	5 (3)	0.626
Neurological			
Coma	23 (7)	6 (4)	0.200
Stoke	7 (2)	2 (1)	0.726
Status epilepticus	11 (3)	5 (3)	0.990
Other neurological reasons (encephalopathy, delirium, etc.)	22 (6)	4 (3)	0.071
Interventional procedure	53 (15)	15 (10)	0.074
Resuscitated cardiac arrest	19 (6)	10 (6)	0.712
Trauma	20 (6)	2 (1)	**0.021**
SBT method			
T-tube	164 (48)	93 (59)	**0.018**
PSV-PEEP	58 (17)	22 (14)	0.412
PSV-ZEEP	121 (35)	42 (27)	0.059
Medical history (n, %)			
COPD	36 (10)	23 (15)	0.181
Hypertension	187 (55)	96 (61)	0.165
Diabetes mellitus	51 (15)	31 (20)	0.172
Previous cardiomyopathy	117 (34)	59 (38)	0.451
LVEF at baseline (328 *vs.* 153) (%)	59 (45–60)	55 (50–60)	0.061
ARDS (n, %)	64 (19)	127 (81)	**< 0.001**
ICU mortality (n, %)	33 (10)	30 (19)	**0.003**

Bold values indicate statistical significance

ARDS acute respiratory distress syndrome, *ARF* acute respiratory failure, *BMI* body mass index, *COPD* chronic obstructive pulmonary oedema, *ICU* intensive care unit, *LVEF* left ventricular ejection fraction, *SAPS II* simplified acute physiology score II, *SBT* spontaneous breathing trial, *SOFA* sequential organ failure assessment

(83%) of patients, "difficult" in 47 (9%) patients, and "prolonged" in 39 (8%) patients (Fig. 1, Supplemental Figure S1). In 53 (8%) cases, the SBT was successful but clinicians in charge decided not to extubate the patient.

Eighty-four (17%) patients underwent more than one SBT (2 (2–3) SBTs per patient) accounting for a total of 218 SBTs (34% of all studied SBTs). Among them, nine (11%) patients experienced WIPO more than once. Among these patients, 29 (36%) had pre-existing cardiomyopathy, eight (10%) suffered from COPD, and 62 (74%) failed SBT at least once, which in total represented 122 SBTs (56% of all failing SBTs).

Compared to patients who never experienced any weaning failure, patients with ≥1 failing SBT were less often males and more often intubated for acute respiratory failure or neurological reasons. Their ICU mortality was significantly higher (Table 1).

Compared to SBTs that succeeded, SBTs that failed were more often performed on a T-piece or under PSV-ZEEP, were performed after more days of mechanical

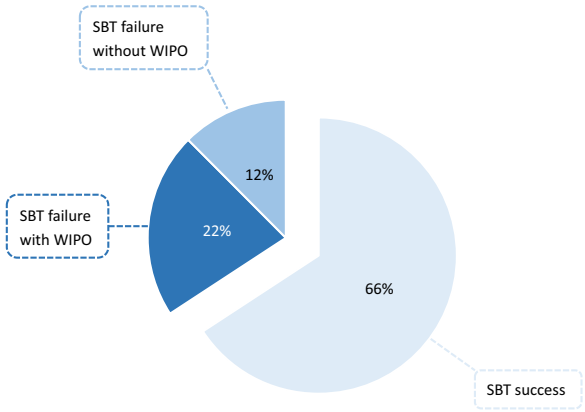

Fig. 1 Incidence of failure of the spontaneous breathing trial (SBT) and weaning-induced pulmonary oedema (WIPO). N = 500 patients

ventilation and after a larger body weight gain (Supplemental Table S3). Altogether, failure occurred in 144/358 (40%) T-piece SBTs, in 25/84 (30%) PSV-PEEP SBTs (p = 0.08 *vs.* T-piece) and in 48/192 (25%) PSV-ZEEP SBTs (p < 0.01 *vs.* T-piece).

The variables included in the multilevel analysis are shown in Supplemental Table S4. Including 551 SBTs from 421 patients, considering both the SBT variables and patient characteristics, identified that T-piece SBT (OR: 2.01 (1.29–3.14), $p = 0.002$), the occurrence of ARDS (OR: 2.81 (1.68–4.68), $p < 0.001$) and the weight gain from the administration to the day of SBT (OR: 1.03 (1.00–1.06) per kg, $p = 0.041$) were associated with weaning failure (Supplemental Table S4). The predictive model constructed on these three factors predicted ≥ 1 weaning failure in these patients with an AUROC of 0.795 (0.756–0.834), (p < 0.01 *vs.* 0.50) (Supplemental Figure S2).

Incidence of WIPO

Consensus on WIPO diagnosis was obtained in all cases (Supplemental appendix, Table S12). WIPO was diagnosed in 79 cases, representing 12% of the 634 SBTs performed and 36% of the 217 failed SBTs (Fig. 1). All SBTs with WIPO failed. The changes in E/e' ratio, in haemoglobin levels, in plasma protein concentration are presented in Supplemental Table S5. Modification in electrocardiogram (T wave inversion) was observed in 1/79 case of WIPO.

Among the 157 patients who failed the SBT at least once (31% of the total population), 59 (38%) presented ≥ 1 failing SBT due to WIPO (Supplemental Table S6). Compared to patients who did not present WIPO, patients who presented ≥ 1 failing SBT due to WIPO had a higher SAPS II on admission, presented more ARDS, more COPD, more hypertension, and more previous cardiomyopathy (Table 2). Among patients with COPD (n = 59), and any type of cardiomyopathy (n = 176), a failing SBT was associated with WIPO in 16/23 (70%), and 33/59 (51%) cases, respectively (Fig. 2).

Compared to SBTs without WIPO, SBTs with WIPO were more often performed under vasopressors (28 (20%) vs. 7 (9%), $p = 0.03$) (Supplemental Table S7). WIPO occurred in 54/358 (15%) T-piece SBTs, in 7/84 (8%) PSV-PEEP SBTs (p = 0.08 *vs.* T-piece SBTs) and 18/192 (9%) PSV-ZEEP SBTs ($p < 0.01$ *vs.* T-piece SBTs). At least one episode of WIPO occurred in 29/414 (7%) patients with "simple" weaning, 14/47 (30%) patients with "difficult" weaning, and 15/39 (38%) patients with "prolonged" weaning.

The incidence of weaning failure ($p < 0.001$) and WIPO ($p < 0.001$) was significantly different across medical, surgical and mixed ICUs (Supplemental Tables S8–S9). Weaning failure was notably higher in the medical ICU compared to the other two types of ICUs ($p < 0.001$). The incidence of WIPO was similar among all three types of ICUs (Supplemental Tables S10–S11).

The multilevel analysis including 202 SBTs from 149 different patients, considering both the WIPO variables and patient characteristics found that COPD (OR: 13.22 (3.08–56.67), $p = 0.001$) and previous cardiomyopathy (OR: 3.97 (1.54–10.23), $p = 0.004$) (Table 3) were independent risk factors for WIPO. The predictive model constructed on these two factors predicted ≥ 1 episode of WIPO in these patients with an AUROC of 0.834 (0.778–0.890), ($p < 0.01$ *vs.* 0.50) (Supplemental Figure S3).

Discussion

This multicentre observational study including 500 patients and 634 SBTs showed that, in a mixed population of critically ill patients, WIPO accounts for 36% of weaning failure. The multivariable analysis showed that COPD, and previous cardiomyopathy were independent risk factors for WIPO as the cause of weaning failure. In patients with COPD and previous cardiomyopathy, WIPO was associated with weaning failure in 70% and 51% of cases, respectively.

The transfer from positive to negative pressure ventilation during SBT worsens the loading conditions of both ventricles, which may induce cardiac dysfunction and WIPO, as it has been evidenced by means of pulmonary artery catheter more than 30 years ago [6]. However, the incidence of the phenomenon is largely unknown, because studies that investigated it were of small size [7, 11] or included specific populations [9, 12, 14, 16–18]. The major strength of the present study is that it was conducted in a large cohort of critically ill patients, admitted for various surgical and medical reasons. A previous study of our group reported a higher incidence of WIPO (59% of failing SBTs) [18]. This may be due to two main

Table 2 Comparison of patient characteristics between patients with and without weaning-induced pulmonary oedema among patients who failed at least once the spontaneous breathing trial

Variables	WIPO − N = 98	WIPO + N = 59	*p*-value
Age (y.o.)	62 (54–72)	66 (59–75)	0.096
Male (n, %)	52 (53,1)	35 (59,3)	0.445
SOFA score	8 (5–11)	8 (6–11)	0.785
SAPS II score	50 (42–64)	63 (43–72)	**0.044**
BMI (kg/m^2)	27,4 (23,0–31,5)	25.1 (23.0–31.0)	0.279
Duration of MV before the SBT (mins)	6 (3–9)	7 (4–11)	0.192
Duration of weaning procedures (mins)	60 (31–68)	60 (32–60)	0.465
Indication of intubation (n, %)			
ARF/shock			
Acute respiratory failure/sepsis/shock	54 (55)	38 (64)	0.252
Septic shock without pneumonia	14 (14)	2 (3)	**0.029**
Other shock types (hypovolaemic, cardiogenic, and vasoplegic non-septic)	2 (2)	3 (5)	0.365
Neurological			
Coma	4 (4)	2 (3)	1.000
Stoke	1 (1)	1 (2)	1.000
Status epilepticus	4 (4)	1 (2)	0.651
Other neurological reasons (encephalopathy, delirium, etc.)	2 (2)	2 (3)	0.632
Interventional procedure	11 (11)	4 (7)	0.359
Resuscitated cardiac arrest	4 (4)	6 (10)	0.178
Trauma	2 (2)	0 (0)	0.528
SBT method			
T-tube	57 (58)	36 (61)	0.725
PSV-PEEP	16 (16)	6 (10)	0.282
PSV-ZEEP	25 (26)	17 (29)	0.651
Medical history (n, %)			
COPD	7 (7)	16 (27)	**0.001**
Hypertension	54 (55)	42 (71)	**0.045**
Diabetes mellitus	19 (19)	12 (20)	0.885
Previous cardiomyopathy	26 (27)	33 (56)	**< 0.001**
LVEF at baseline (94 *vs.* 59) (%)	55 (50–60)	55 (45–60)	0.835
ARDS (n, %)	32 (33)	21 (36)	0.706
ICU mortality (n, %)	18 (18)	12 (20)	0.761

Bold values indicate statistical significance

ARDS acute respiratory distress syndrome, *ARF* acute respiratory failure, *BMI* body mass index, *COPD* chronic obstructive pulmonary oedema, *ICU* intensive care unit, *LVEF* left ventricular ejection fraction, *SAPS II* simplified acute physiology score II, *SBT* spontaneous breathing trial, *SOFA* sequential organ failure assessment, *WIPO* weaning-induced pulmonary oedema

reasons. First, this single-centre study mainly included patients with pneumonia and/or septic shock, in whom the incidence of WIPO is higher than in other types of patients, as shown by the present study. Second, SBTs were performed only with a T-piece in the previous single-centre study, which was also associated with a higher likelihood of WIPO in the present investigation.

The two common independent risk factors of WIPO, as in the above-mentioned previous study [18], in case of a failed SBT, were COPD and previous cardiomyopathy. This is in relationship with the mechanisms of WIPO [5]. During the SBT process, the inspiratory drop in intrathoracic pressure increases the left ventricular preload and afterload, and the rise in transpulmonary pressure due to high-volume ventilation increases the right ventricular afterload [5]. This explains that patients with COPD, in whom airway obstruction induces large negative swings in intrathoracic pressure [6, 28], are particularly at risk of WIPO. Hypertension induced by adrenergic stress and hypercapnia may contribute to the increase in left

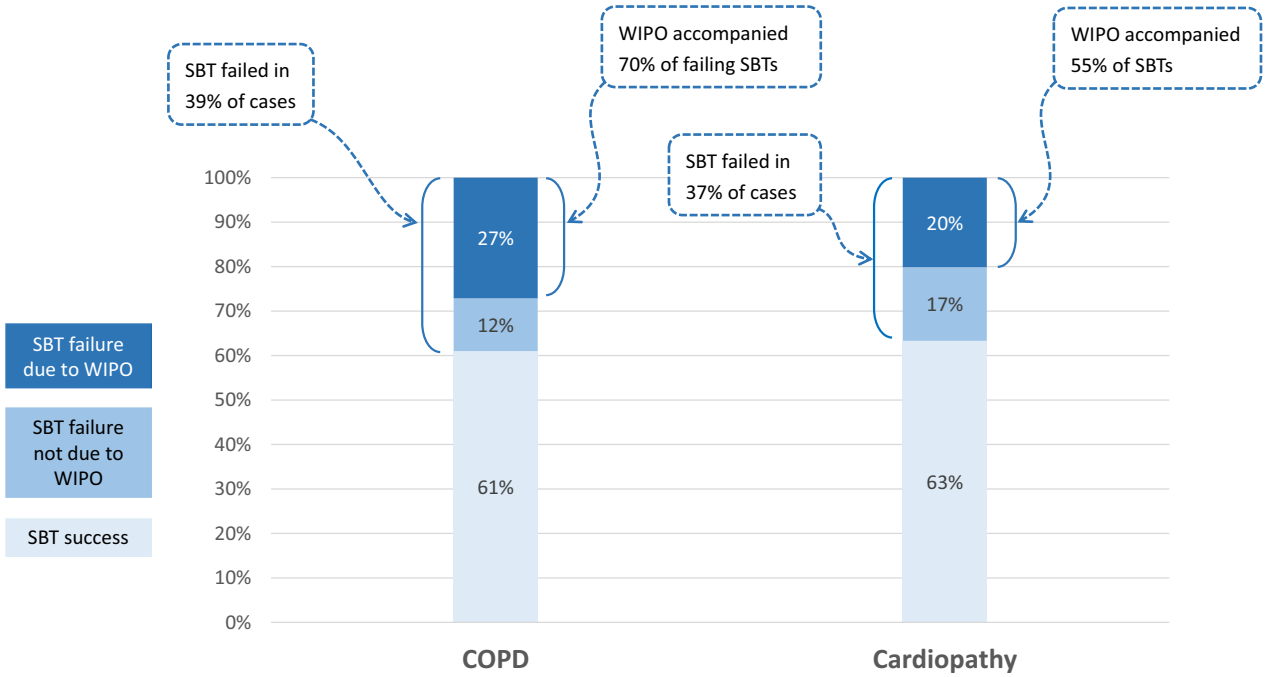

Fig. 2 Incidence of failure of the spontaneous breathing trial (SBT) and weaning-induced pulmonary oedema (WIPO) in patients with chronic obstructive pulmonary disease (COPD) and patients with previous cardiomyopathy. N = 500 patients

Table 3 Multilevel logistic regression analyses based on the presence of weaning-induced pulmonary oedema in patients who failed at least once the spontaneous breathing trial

Variables	Odds ratio	95% CI	*P*-value
(Intercept)	0.08	0.014–0.456	0.004
Male	1.41	0.640–3.096	0.396
Obesity	0.61	0.249–1.509	0.287
SAPS II	1.01	0.988–1.029	0.404
COPD	13.22	3.083–56.672	**0.001**
Previous cardiomyopathy	3.97	1.540–10.229	**0.004**
ARDS	1.58	0.683–3.641	0.286
T-piece	0.71	0.297–1.701	0.444
SBP pre-SBT	1.03	0.975–1.092	0.283
ΔWeight gain	1.03	0.981–1.076	0.257
Use of diuretics	1.44	0.658–3.134	0.363

Bold values indicate statistical significance

ARDS acute respiratory distress syndrome, *COPD* chronic obstructive pulmonary disease, *SAPS II* simplified acute physiology score II, *SBP* systolic blood pressure, *SBT* spontaneous breathing trial

ventricular afterload [6]. The failing left ventricle is more sensitive to changes in its afterload than the normal one [6, 29], explaining that dilated or hypertrophic cardiomyopathy is another risk factor for WIPO. Atrial fibrillation may impede the ability of ventricles to cope with altered loading conditions. Myocardial ischemia, resulting from the imbalance between reduced myocardial oxygen supply and increased oxygen requirements may contribute to WIPO, but the incidence seems quite rare [9, 18]. Accordingly, one case of WIPO only was accompanied with changes in electrocardiogram in the present study.

Eventually, at least one episode of WIPO was associated with a failing SBT in 70% of COPD patients and 56% of patients with previous cardiomyopathy. This suggests that clinicians should specifically look for WIPO in such high-risk patients. This may subsequently promote a specific treatment that should fasten weaning [19]. Of note, obesity, which was identified as a risk factor for WIPO in a previous study [18] was not so in the present one.

Our results indicate that the incidence of ARDS was higher in patients with weaning failure than in the other ones. This may be explained by the fact that patients with ARDS often have persistent lung damage that impedes weaning. They also have had a high-level respiratory assistance, and a long delay before the first separation attempt, two factors that are associated with weaning failure [30]. We also observed an association between respiratory dysfunction, weaning failure, and mortality, which has already been reported [3, 31–33].

In the present study, the proportion of short, difficult, and prolonged weaning was comparable to that reported by other studies in critically ill patients [3]. In multivariate analysis, the patient characteristics independently associated with weaning failure have been already reported by other studies [34, 35].

T-piece, in fact, was regarded as the most challenging for the heart. It induces larger decreases in intrathoracic pressure than in PSV-PEEP and PSV-PEEP trials, and larger increases in the left ventricular filling pressure, as nicely demonstrated in a previous study [11]. Accordingly, in the present study, the incidence of WIPO was higher among failing SBTs performed on a T-piece than with PSV-ZEEP and tended to be higher than with PSV-PEEP, even though the latter modalities were much less used than T-piece. These results may suggest that, in patients at high risk, a T-piece trial would be a more stressful test to detect WIPO before extubation. The lately released randomized controlled trial by Thille et al. [36] showed that, in patients at high risk of reintubation, there is no superiority of PSV-ZEEP over the T-piece method in terms of ventilator-free days at day-28. However, WIPO as a cause of weaning failure was not investigated.

Several limitations of our study deserve consideration. First, the diagnosis of WIPO was made by a group of experts but not with the pulmonary artery catheter, which may be considered a gold standard [5]. However, this invasive technique is today rarely used for the purpose of weaning of mechanical ventilation. The consensual approach used in the current study may introduce individual biases and the possibility of panel-group pressure. Moreover, transthoracic echocardiography, which is a surrogate for estimating the left ventricular filling pressure, was used in the majority of cases [5, 13]. However, we felt that this was the best way to combine the diagnostic value of alternative methods to the pulmonary artery catheter which, taken in isolation, each have different limitations.

Second, other causes of weaning failure were not investigated, such as respiratory, neurologic, or diaphragmatic causes. However, this should not have changed the incidence of WIPO. Third, the study did not investigate the treatments triggered by the diagnosis of WIPO made by the attending clinicians, as it was not our primary goal. Additionally, the differences among centres regarding the timing and method of SBT may have introduced some variability and affected the results. The multivariate logistic regression and exploratory analyses may indicate how differences in the type of ICUs, SBT mode and duration and past medical history influence the incidence of weaning failure and of WIPO. Finally, even though our study was the largest that evaluated the incidence of WIPO, some subgroups may be too small to allow significant comparisons, e.g., regarding the indications for intubation.

Conclusions

In this large mixed population of critically ill patients, WIPO was associated with 36% of weaning failure. Previous heart disease and COPD were two independent risk factors for developing WIPO during the weaning process.

Abbreviations

ARDS	Acute respiratory distress syndrome
COPD	Chronic obstructive pulmonary disease
ICU	Intensive care unit
LVEF	Left ventricular ejection fraction
PEEP	Positive end-expiratory pressure
PSV	Pressure support ventilation
SBT	Spontaneous breathing trial
WIPO	Weaning-induced pulmonary oedema
ZEEP	Zero end-expiratory pressure

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13054-025-05350-6.

Additional file1

Author contributions

RS acquired the data, performed data analysis and interpretation, and wrote the manuscript. SA acquired the data, and contributed to writing the manuscript. MB acquired the data, and contributed to writing the manuscript. RP acquired the data, and contributed to writing the manuscript. ML acquired the data, and contributed to writing the manuscript. NDV acquired the data, and contributed to writing the manuscript. BL acquired the data, and contributed to writing the manuscript. AP acquired the data, and contributed to writing the manuscript. KM acquired the data, and contributed to writing the manuscript. TH acquired the data, and contributed to writing the manuscript. VL acquired the data, and contributed to writing the manuscript. MG acquired the data, and contributed to writing the manuscript. AH acquired the data, and contributed to writing the manuscript. MC acquired the data, and contributed to writing the manuscript. NA performed data analysis and interpretation, and contributed to writing the manuscript. DO performed data analysis and interpretation, and contributed to writing the manuscript. FM acquired the data, and contributed to writing the manuscript. CL acquired the data, and contributed to writing the manuscript. TP performed data analysis and interpretation, and contributed to writing the manuscript. JLT conceived the study, performed data analysis and interpretation, and contributed to writing the manuscript. XM conceived the study, performed data analysis and interpretation, and wrote the manuscript. RS, SA, MB, RP, ML, NDV, BL, AP, KM, VL, MG, AH, MC, NA, DO, FM, CL, TP, JLT and XM reviewed the manuscript and approved its final version.

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Availability of data and materials

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

The trial protocol was approved by the ethics committee of the French Intensive Care Society (2017-A00392-51) and registered on ClinicalTrials (NCT05318261). Informed consent was obtained from each patient or from the patient's legally authorized representative if the patient was unable to provide consent. Alternatively, deferred informed consent was obtained from patients. The current study was performed in accordance with French law and the Declaration of Helsinki.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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