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Pneumothorax in the Intensive Care Unit

Incidence, Risk Factors, and Outcome

Arnaud de Lassence, M.D., Jean-François Timsit, M.D., Ph.D.,† Muriel Tafflet, M.Sc.,‡ Élie Azoulay, M.D., Ph.D.,§ Samir Jamali, M.D.,‖ François Vincent, M.D.,# Yves Cohen, M.D.,** Maïté Garrouste-Orgeas, M.D.,†† Corinne Alberti, M.D., Ph.D.,‡‡ Didier Dreyfuss, M.D.,§§ on behalf of the OUTCOMEREA® Study Group* ‖‖

Background: **The risk factors and outcomes of critically ill patients with iatrogenic pneumothorax (IP) have not been studied in a large unselected intensive care unit (ICU) population.**

Methods: **The authors studied a prospective cohort of adults admitted for more than 24 h. Data were collected at ICU admission and daily by senior physicians until ICU discharge. Risk factors for IP were identified in the entire cohort. A matched nested case–control study was used to evaluate the excess risk of IP in decedents.**

Results: **Of the 3,499 patients, 69 with pneumothorax before ICU admission were excluded. Of the remaining 3,430 patients, 94 experienced IP within 30 days (42 due to barotrauma and 52 due to invasive procedures). The cumulative incidence of IP was 1.4% (95% confidence interval [CI], 1.0–1.8) on day 5 and 3.0% (95% CI, 2.4–3.6) on day 30. Risk factors for IP (hazard ratio [95% CI]) were body weight less than 80 kg (2.4 [1.3–4.2]), history of adult immunodeficiency syndrome (2.8 [1.2–6.4]), diagnosis of acute respiratory distress syndrome (5.3 [2.6–11]) or cardiogenic pulmonary edema at admission (2.0 [1.1–3.6]), central vein or pulmonary artery catheter insertion (1.7 [1.0–2.7]), and use of inotropic agents during the first 24 h (2.1 [1.3–3.4]). Excess risk of IP in decedents was 2.6 (95% CI, 1.3–4.9; $P = 0.004$).**

Conclusion: **Iatrogenic pneumothorax is a life-threatening complication seen in 3% of ICU patients. Incorporating risk factors for IP into preventive strategies should reduce the occurrence of IP.**

IATROGENIC pneumothorax (IP) is one of the main iatrogenic complications in intensive care unit (ICU) patients.[1] The incidence of IP in the ICU was greater than 20% in the 1990s[2–8] and has since decreased to 3%.[9,10] IP in the ICU occurs chiefly as a complication of barotrauma related to mechanical ventilation (IP-MV) or as a postprocedural event (*e.g.*, after central venous catheter insertion, thoracentesis, or surgery). Most studies of the prognosis and outcome of IP were retrospective and focused on a single category of IP.[9,11–17]

The development of lung-protective strategies for ventilation and of new material, techniques, and recommendations for inserting central vein catheters makes IP largely preventable in routine practice.[18] Nevertheless, the occurrence of IP is closely related to the underlying disease, such as adult respiratory distress syndrome (ARDS) for IP-MV. Identifying patients with risk factors in order to take specific preventive steps may be beneficial.

The aim of this study was to investigate the incidence, risk factors, morbidity, and mortality of IP in the large OUTCOMEREA® database.

Materials and Methods

Database

We conducted a prospective observational study in a multicenter database (OUTCOMEREA®) from January 1997 to June 2003. The database, fed by 11 French medical or surgical ICUs, is specifically designed to record daily disease severity and occurrence of iatrogenic events and nosocomial infections. A random sample of patients older than 16 yr and having ICU stays longer than 24 h was entered into the database each year. Briefly, the center could choose among two methods for random sampling: (1) consecutive admissions in n ICU beds or (2) consecutive admissions in a given month. Beds (or month) were allocated to the database once a year by the database steering committee. We studied all patients in the OUTCOMEREA® database except those admitted to the ICU for pneumothorax (n = 69).

Method of Data Collection. Data were collected daily by senior physicians in each participating unit. For each patient, the investigator entered the data into a computer case-report form using the data capture software VIGIREA® (OUTCOMEREA; Rosny sous bois, France) and imported all records to the OUTCOMEREA® database. All codes and definitions were established before study initiation.

* Attending Physician, §§ Professor, Medical Intensive Care Unit, Assistance Publique-Hôpitaux de Paris, Louis Mourier Teaching Hospital, Colombes, France. † Professor, Group of Epidemiology, Institut National de la Santé et de la Recherche Médicale (INSERM) U578, Grenoble, France, and Medical Intensive Care Unit, Assistance Publique-Hôpitaux de Paris, Bichat-Claude Bernard Teaching Hospital, Paris, France. ‡ Research Assistant, Department of Biostatistics, OUTCOMEREA® Organization, Rosny sous bois, France. § Professor, Medical Intensive Care Unit, Assistance Publique-Hôpitaux de Paris, Saint Louis Teaching Hospital, Paris, France. ‖ Attending Physician, Polyvalent Intensive Care Unit, Centre Hospitalier de Dourdan, Dourdan, France. # Attending Physician, Renal Intensive Care Unit, Assistance Publique-Hôpitaux de Paris, Tenon Teaching Hospital, Paris, France. ** Professor, Medical-Surgical Intensive Care Unit, Assistance Publique-Hôpitaux de Paris, Avicenne Teaching Hospital, Bobigny, France. †† Attending Physician, Medical-Surgical Intensive Care Unit, Saint Joseph Teaching Hospital, Paris, France. ‡‡ Associate Professor, Department of Epidemiology, Assistance Publique-Hôpitaux de Paris, Hôpital Robert Debré, Paris France. ‖‖ The members of the OUTCOMEREA® Study Group are listed in the appendix.

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Address reprint requests to Dr. Timsit: Group of Epidemiology, Institut National de la Santé et de la Recherche Médicale (INSERM) U578 and Service de Réanimation Médicale, University Hospital Grenoble, 38043, Grenoble, Cedex France. Address electronic mail to: jf.timsit@outcomerea.org. Individual article reprints may be purchased through the Journal Web site, www.anesthesiology.org.

Procedures. All study ICUs followed the same rules for mechanical ventilation and catheter insertion. In mechanically ventilated patients, tidal volume was set to maintain a plateau pressure below 30 cm H_2O in most cases and no greater than 35 cm H_2O in all patients.[19]

Central venous access was chosen according to a previously suggested algorithm.[20] Briefly, to avoid catheter-related infection, subclavian access was preferred except in patients with severe hemostasis disorders or arterial oxygen tension (Pao_2)/fraction of inspired oxygen (Fio_2) less than 150, in whom the choice between the femoral and internal jugular routes was at the discretion of the attending physician. Written protocols were shared among the participating ICUs, but practices were not audited.

Study Variables. The following data were recorded: patient characteristics at admission (age, sex, origin, and body weight), admission diagnosis (pneumonia, cardiogenic pulmonary edema, acute exacerbation of chronic obstructive pulmonary disease, or ARDS[21]), admission category, main symptom, diabetes, acquired immunodeficiency syndrome (AIDS),[22] chronic diseases,[23] McCabe score,[24] main clinical features and laboratory findings, treatment modalities (most notably mechanical ventilation [yes/no] and endotracheal mechanical ventilation [yes/no], inotropic agents, and antimicrobials), and catheters. The following scores were computed at admission and daily thereafter: Simplified Acute Physiologic Score (SAPS II),[25] Logistic Organ Dysfunction (LOD),[26] Sequential Organ Failure Assessment,[27] and Glasgow Coma Scale score. Last, duration of invasive ventilation, duration of ICU and hospital stays, and outcomes at ICU and hospital discharges were recorded.

Quality of the Database. Data were collected daily on computers by ICU physicians closely involved in establishing the database. The software immediately conducts an automatic check of most of the variables entered by the investigator. Multiple automatic checking of internal consistency generated queries that were sent to the ICUs before the new data were incorporated into the database. At each study ICU, the quality control procedure involved having a senior ICU physician from another study ICU check a 2% random sample of study data. Interrater correlation coefficients ranged from 0.67 to 1 for clinical variables, severity scores, and organ dysfunction scores, and κ coefficients for qualitative variables ranged from 0.5 to 0.9. Missing values occurred only for age and weight (less than 1% of the cohort), which were replaced by median sex-specific values.

IP Definitions. Chest radiographs were obtained at least once a day during the first month in all ventilated patients, routinely after thoracentesis or central venous catheter insertion, and when clinically indicated. Computed tomography was performed when the chest radiograph did not confirm a clinically suspected diagnosis. IP was also diagnosed when drainage of a tension pneumothorax was required before chest radiography.

All patients were screened daily for IP throughout the ICU stay. Four categories of IP were distinguished: IP secondary to barotrauma caused by invasive mechanical ventilation (IP-MV), IP after central venous catheter insertion (IP-CVC), IP after thoracentesis, and IP related to other causes.

Statistical Analysis

Quantitative and qualitative variables are reported as medians [interquartile range (IQR)] and n (%), respectively. We studied the incidence of first IP (within the first 30 days), taking "discharge from the ICU alive without experiencing IP" as a competing risk. We used the cumulative incidence instead of Kaplan-Meier plots.[28]

The first episode of IP within the first 30 days in the ICU was considered. A proportional hazard model was used to compute the time to IP and to investigate risk factors for IP. We used the Fine and Gray extension of the Cox model to take competing risks into account.[29]

Variables significantly associated with IP at a 0.05 level of risk were selected using a bivariate Cox model. Multivariate analysis was performed with stepwise forward selection. Because we anticipated colinearity between severity and organ dysfunction scores, these were introduced successively at the first step of the multivariate analysis.

The proportional risk and log-linearity hypotheses were checked for all models. For continuous variables, when log linearity was not confirmed, we cut variables on the break points of the spline curves. A pooled two-way interaction test was used to unmask significant interactions between variables in the final model. Results are reported as hazard ratios and 95% confidence intervals (CIs).

A pneumothorax risk score was developed from the regression coefficients associated with each variable. Internal validation of the pneumothorax risk score was performed by bootstrapping, which involves analyzing a large number (400 independent replicates) of subsamples with replacement from the full sample. Bootstrapping provides nearly unbiased estimates of β coefficients of the final regression. External validation was also performed using an external data set of patients included in the database between June 2003 and November 2004 (n = 1,798).

Hospital mortality rate in patients with IP, invasive ventilation on the day of IP occurrence, duration of stay before and after IP, mortality after IP, and changes in daily LOD before and after IP were studied consecutively.

We investigated whether the risk of IP was increased in decedents, taking into account confounding factors such as severity and duration of ICU stay. To this end, we designed a nested case–control study comparing patients who died in the hospital and patients who were

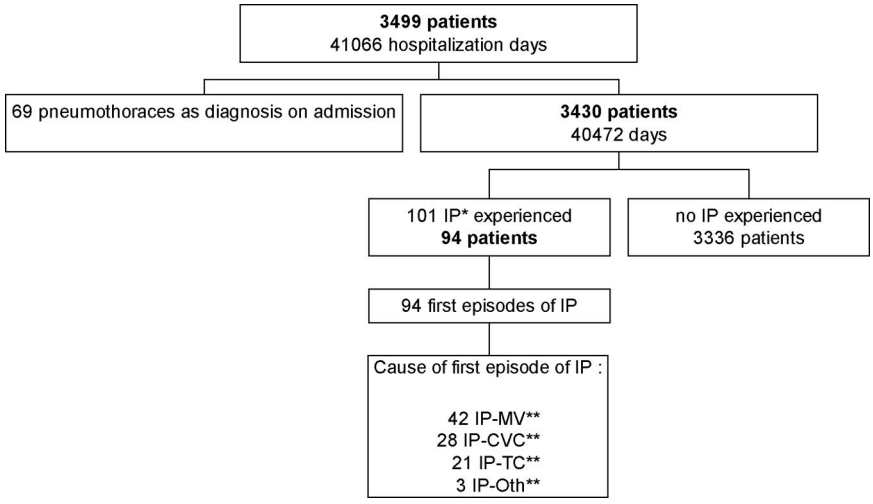

Fig. 1. Flow diagram of the study. * Iatrogenic pneumothorax (IP) before 30 days in intensive care unit. ** IP-CVC = IP after central venous catheter; IP-MV = IP secondary to barotrauma under invasive ventilation; IP-Oth = other cause of IP; IP-TC = IP after thoracentesis.

discharged alive from the hospital. At least 631 cases and controls were needed to detect an increase in the odds ratio (OR) for IP of 2 assuming a 3% IP prevalence in survivors (with α 0.05 and β 0.20). The case–control (1:1) matching criteria were probability of hospital death (SAPS II) ± 5%, duration of ICU stay ± 20%, invasive ventilation at admission, and transfer from a ward.##

We used conditional logistic regression with and without adjustment on matching criteria, risk factors for death, and risk factors for IP. Clinically relevant two-way interactions were selected in the final model and tested.

Sensitivity analyses of the IP risk were performed in patients ventilated for at least 24 h, in those with intermediary SAPS II values (27–48 points, *i.e.*, from the 25th to the 75th percentiles), and in those without decisions to forego life-sustaining treatments (withdrawal or withholding decisions taken by consensus among ICU staff members and communicated to intensivists on duty or written in the patient's medical record).

All statistical tests were two tailed, and *P* values less than 0.05 were considered significant. All statistical analyses were performed using the SAS 8.02 software package (SAS Inc., Cary, NC) and S-plus 2000 (MathSoft Inc., Seattle, WA).

Results

Study Population

Of the 10,339 patients admitted to all OUTCOMEREA® ICUs during the study period, 3,430 (29%) were enrolled in the 11 participating ICUs (40,472 ICU days). Among these, 94 (2.7%; 95% CI, 2.2–3.2%) experienced at least one episode of IP within the first 30 days (fig. 1); 7 patients had two episodes (including 1 episode on day 31).

Among the 3,430 study patients, 2,299 (67%) received invasive mechanical ventilation for at least 24 h and 1,949 (57%) for at least 48 h. IP was associated with longer durations of the ICU stay (7 [IQR, 4–13] *vs.* 17.5 [IQR, 9–32] days; $P < 0.001$) and hospital stay (18 [IQR, 10–33] *vs.* 31 [IQR, 14–46] days; $P < 0.001$). Mortality rates in the ICU (22 *vs.* 45%; $P < 0.001$) and hospital (28 *vs.* 51%; $P < 0.001$) were also higher in patients with IP.

Incidence and Epidemiology of IP

The first episode of IP was secondary to barotrauma during invasive ventilation (IP-MV) in 42 patients, with a median time from admission to IP of 5 days [IQR, 3–10 days] and from mechanical ventilation initiation to IP of 4 days [IQR, 2–8 days]. IP followed central venous catheter insertion (IP-CVC) in 28 patients, with a median time from admission to IP of 3.5 days [IQR, 2.5–9 days]. IP occurred after thoracentesis in 21 patients, with a median time from admission to IP of 7 days [IQR, 3–12 days]. IP was due to other causes in 3 patients, with a median time from admission to IP of 20 days [IQR, 10–26 days]. Overall, the median time from admission to the first episode of IP was 5.5 days [IQR, 3–11 days].

The cumulative incidence of IP was 1.4% (95% CI, 1.0–1.8) on day 5, 2.1% (95% CI, 1.6–2.6) on day 10, and 3.0% (95% CI, 2.4–3.6) on day 30 (fig. 2). On day 30, cumulative incidences were as follows: IP-MV, 1.3% (95% CI, 0.9–1.7); IP-CVC, 0.9% (95% CI, 0.5–1.2); and IP after thoracocentesis, 0.7% (95% CI, 0.4–1.0).

Disease severity according to SAPS II, LOD, and Sequential Organ Failure Assessment values was greater in the patients with IP (table 1). A larger proportion of patients with than without IP had AIDS, pneumonia at admission, pulmonary edema, or ARDS. Patients with IP were more likely to receive invasive ventilation and to require insertion of arterial, central, and pulmonary artery catheters.

Of the 94 patients with IP, 10 died on the same day of or the day after the event. Tension IP caused cardiac arrest in 10 patients (10.6%).

SAS macro procedure. Available at: http://www.outcomerea.org/ehtm/matchmacro.pdf. Accessed September 30, 2005.

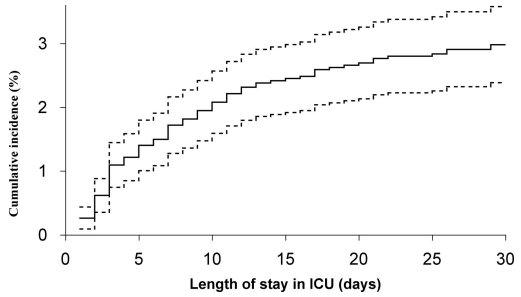

Fig. 2. Delay occurrence of the first iatrogenic pneumothorax and 95% confidence intervals. This diagram represents the cumulative incidence while the event "leaving intensive care unit (ICU) alive without iatrogenic pneumothorax" is considered to be a competing risk.

Chest tube drainage was required in 87 patients (93%), for a median duration of 6 days [3–10 days]. The medical records of the remaining 7 patients were reviewed retrospectively by the attending physicians. Two of these patients had severe hemostasis disorders and experienced localized IP after being weaned off mechanical ventilation. In the other 5 patients, localized IP occurred during spontaneous breathing, after thoracentesis (n = 2), central vein catheter insertion (n = 2), or transbronchial biopsy (n = 1) and resolved with oxygen therapy.

Severity according to LOD values increased significantly between the day before and the day after IP. The mean LOD score increase was +0.59 [+0.13 to +1.05], $P = 0.004$, on the day of IP and +1.38 [+0.57 to +1.86], $P < 0.001$, on the day after IP.

Risk Factors for IP

The univariate and multivariate analyses of risk factors for IP are reported in tables 1 and 2. At the last step of the multivariate analysis, six factors were independently associated with IP: history of AIDS, diagnosis of cardiogenic pulmonary edema at admission, diagnosis of ARDS at admission, insertion during the first 24 h of a central vein catheter or pulmonary artery catheter, and use of vasoactive agents during the first 24 h (table 2). Bootstrap analysis did not influence the type or significance of the independent risk factors (table 2).

The risk factors for IP showed little change when the analysis was rerun on mechanically ventilated patients only or on patients with at least one central venous catheter or with a pulmonary artery catheter. AIDS was a risk factor for IP-MV but not for IP-CVC.

Based on the adjusted hazards ratios of variables included in the final model, an IP risk score was built (table 3). This score could range from 0 to 6. Two points were assigned to ARDS at admission, and one point was assigned to each of the other risk factors. The cumulative incidence of IP according to the risk score is shown in figure 3. The cumulative risk on day 30 ranged from 0.9% (95% CI, 0–1.9%) with a score of zero to 34% (95% CI, 9.5–59%) with a score of 5 or greater (fig. 3A). The model was tested on an external data set based on a more recent population entered in the database (n = 1,798 patients). Thirty-two IPs occurred (1.9%). As shown in figure 3B, the risk of IP within the first 30 days in this external population was 0% when the IP risk score was 0, 9.1% when the risk score was 4, and 15.1% when the risk score was 5 or 6.

Increased Risk of IP in Decedents: Case–Control Study

Among the 982 decedents, 745 were successfully matched with a survivor. The adequacy of matching was 100% for the probability of hospital death according to SAPS II at admission and ICU duration of stay, 87% for invasive ventilation, and 83% for transfer from ward. In the 745 matched pairs (1,490 patients), 39 IPs (5.2%) occurred in decedents, and 17 (2.2%) occurred in survivors ($P = 0.003$). The population enrolled in the nested case–control study is shown in table 4.

Multivariate Analysis: Conditional Logistic Regression

In the multivariate analysis, we took into account all variables used for matching and several additional variables expected to affect outcome, such as LOD, chronic diseases, admission category, and age, as well as risk factors for IP such as an admission diagnosis of pneumonia, pulmonary edema, or ARDS; body weight; pulmonary artery or central catheter insertion; and AIDS. Clinically relevant two-way interactions were also tested (LOD with age, chronic disease, body weight < 80 kg, unscheduled surgery, and invasive ventilation; diagnosis of pneumonia with unscheduled surgery; and chronic disease with unscheduled surgery, hospital death probability, and body weight).

Iatrogenic pneumothorax was more common in decedents: The unadjusted OR was 2.37 (95% CI, 1.32–4.26; $P = 0.0028$), and the OR adjusted on the above-listed variables was 2.56 (95% CI, 1.34–4.89; $P = 0.0043$).

Finally, the excess risk of death associated with IP-MV (OR, 2.44; 95% CI, 0.96–6.24) was not different from that associated with IP-CVC (OR, 2.67; 95% CI, 1.1–6.45).

The estimated excess risk of death was unchanged in separate analyses of ventilated patients (530 pairs; OR, 2.68; 95% CI, 1.32–5.45; $P = 0.0065$), patients with intermediate severity (SAPS II between 27 and 48; 254 pairs; OR, 3.19; 95% CI, 0.98–10.4; $P = 0.055$), and patients without decisions to forego life-sustaining treatment (450 pairs; OR, 2.72; 95% CI, 1.08–7.22; $P = 0.032$).

Discussion

The results from this large multicenter study show that IP is a life-threatening complication associated with a

Table 1. Characteristics of Patients Enrolled in the Study

	Patients with No IP* (n = 3,336)	Patients with IP* (n = 94)	HR [95% CI]	*P* Value
Age, yr	64 (49–74)	63 (51–77)	1.0 [0.9–1.0]	0.6
Male sex	2,072 (62.1)	65 (69.1)	1.3 [0.8–2.0]	0.2
Weight < 50 kg	263 (7.9)	14 (14.9)	1.7 [1.0–3.1]	0.06
50 ≤ Weight < 80 kg	2,229 (66.8)	67 (71.3)	1	
Weight ≥ 80 kg	844 (25.3)	13 (13.8)	0.5 [0.3–0.9]	0.02
SAPS II on first day	37 (27–48)	40 (30–54)	1.02 [1.01–1.03]	0.001
LOD on first day	4 (2–6)	4.5 (2–6)	1.10 [1.03–1.17]	0.03
SOFA on first day	5 (3–7)	6 (3–9)	1.12 [1.06–1.18]	0.001
Admission category				
Medical	2,388 (71.6)	66 (70.2)	0.7 [0.4–1.3]	0.3
Scheduled surgery	398 (11.9)	15 (16.0)	1	
Unscheduled surgery	550 (16.5)	13 (13.8)	0.6 [0.3–1.3]	0.2
Transfer from ward	1,669 (50.0)	55 (55.6)	1.0 [0.6–1.6]	0.4
Chronic diseases (several possible diseases per patient)				
Cirrhosis	209 (6.3)	5 (5.3)	0.8 [0.3–2.1]	0.7
Cardiovascular insufficiency	478 (14.3)	16 (17.0)	1.2 [0.7–2.1]	0.4
Respiratory insufficiency	610 (18.3)	18 (19.1)	1.1 [0.6–1.8]	0.8
Renal Insufficiency	135 (4.1)	1 (1.1)	0.3 [0.03–1.8]	0.2
Immunosuppression	455 (13.7)	11 (11.7)	0.8 [0.4–1.6]	0.6
AIDS	85 (2.6)	6 (6.4)	2.5 [1.1–5.8]	0.03
Diagnosis at admission				
Pneumonia	596 (17.9)	34 (36.2)	2.5 [1.7–3.9]	< 0.001
Cardiogenic pulmonary edema	272 (8.1)	13 (13.8)	1.7 [0.9–3.1]	0.06
COPD	247 (7.4)	3 (3.2)	0.4 [0.1–1.3]	0.1
ARDS	58 (1.7)	8 (8.5)	6.0 [2.9–12.4]	< 0.001
Main symptom at admission				
Shock (all cause)	641 (19.2)	23 (24.5)	5.0 [1.5–16.8]	0.008
Multiple organ failure	119 (3.6)	3 (3.2)	3.5 [0.7–17.6]	0.06
Respiratory failure	906 (27.2)	40 (42.5)	6.2 [1.9–20]	0.002
COPD	203 (6.1)	5 (5.3)	3.5 [0.8–4.5]	0.09
Acute renal failure	205 (6.2)	1 (1.1)	0.7 [0.1–6.7]	0.8
Coma	537 (16.1)	10 (10.6)	2.6 [0.7–9.6]	0.1
Scheduled surgery	254 (7.6)	8 (8.5)	4.4 [1.2–16.8]	0.03
Trauma	44 (1.3)	1 (1.1)	3.2 [0.3–30.6]	0.3
Other	427 (12.8)	3 (3.2)	1	
Use during the first day of ICU				
Invasive ventilation	1,760 (52.8)	64 (68.1)	1.9 [1.2–2.9]	0.004
Noninvasive ventilation	214 (6.4)	4 (4.3)	0.6 [0.2–1.8]	0.4
Pa_{O_2}/F_{IO_2} for patients under invasive ventilation, mmHg†	238 (153–350)	191 (120–286)	0.997 [0.995–0.999]	0.01
Inotropic support‡	1,030 (30.9)	50 (53.2)	2.5 [1.7–3.8]	< 0.001
Arterial catheter	584 (17.5)	26 (27.7)	1.8 [1.1–2.8]	0.01
Swan-Ganz or central venous catheters	1,214 (36.4)	53 (56.4)	2.2 [1.5–3.4]	< 0.001
Corticosteroids§	459 (13.8)	13 (13.8)	1.0 [0.5–1.8]	0.9

Cardiogenic pulmonary edema is defined according to the opinion of the investigators according to clinical examination, echocardiographic results, and evolution.

* Iatrogenic pneumothorax (IP) before 30 days in intensive care unit (ICU). † 1,824 patients ventilated during the first ICU day. ‡ Use of dobutamine, dopamine > 5 $\gamma \cdot kg^{-1} \cdot min^{-1}$, epinephrine, or norepinephrine. § Use of at least 0.5 mg · kg $^{-1}$ · day^{-1} prednisone, 2.5 mg · kg $^{-1}$ · day^{-1} hydrocortisone, or 0.1 mg · kg $^{-1}$ · day^{-1} methylprednisolone.

AIDS = acquired immunodeficiency syndrome; ARDS = acute respiratory distress syndrome; CI = confidence interval; COPD = chronic obstructive pulmonary diseases; F_{IO_2} = fraction of inspired oxygen; HR = hazard ratio; LOD = Logistic Organ Dysfunction; Pa_{O_2} = arterial oxygen tension; SAPS = Simplified Acute Physiology Score; SOFA = Sequential Organ Failure Assessment.

more than twofold increase in the risk of death. The 30-day incidence of IP was 3% in the overall population. The occurrence of IP was heavily dependent on risk factors that can be easily collected at ICU admission.

The overall incidence of IP secondary to mechanical ventilation in ICUs is not well known because most of the published studies investigated barotrauma related to mechanical ventilation without distinguishing clearly among pneumothorax, pneumomediastinum, pneumoperitoneum, and subcutaneous emphysema.[1,5,9,11,17,21,30] Furthermore, postprocedural IP was either not taken into account or lumped together with other mechanical procedure-related events such as hemorrhage, faulty catheter position, or failure of a central venous catheter.[11,17]

The overall rate of IP in ICU patients was 8% in the 1980s[2] and subsequently decreased to 3–4%.[1,10] Even in recent series, however, the incidence rate of pneumothorax was as high as 7–14% in patients receiving mechanical ventilation[5,9,16] and was highest in patients with acute lung injury and ARDS.[12,15,30–33] Mechanical ventilation was the most common cause of IP in our series, in keeping with previous reports[9,15] However,

Table 2. Risk Factors for IP: Multivariate Analyses

	n (%)	Hazard Ratio [95% CI]	95% CI*	*P* Value
Model 1: overall population, n = 3,430				
Number of IPs studied before 30 days: 94				
Weight < 80 kg	2,573 (75.0)	2.35 [1.30–4.22]	1.28–4.2	0.004
AIDS	91 (2.6)	2.77 [1.20–6.41]	1.20–7.02	0.02
Diagnosis of cardiogenic pulmonary edema	285 (8.3)	1.96 [1.08–3.55]	1.06–3.54	0.03
Diagnosis of ARDS	66 (1.9)	5.34 [2.56–11.14]	2.55–13.03	< 0.001
Inotropic support on first day	1,080 (31.5)	2.13 [1.33–3.42]	1.26–3.42	0.0017
Central venous or pulmonary artery catheters on first day	1,267 (36.9)	1.64 [1.02–2.65]	1.00–2.63	0.04
Model 2: ventilated patients (at least 24 h), n = 2,299				
Number of IPs occurred with VM studied before 30 days: 77				
Weight < 80 kg	1,666 (72.5)	2.06 [1.11–3.85]	1.09–3.87	0.02
AIDS	55 (2.4)	3.06 [1.30–7.23]	1.25–7.33	0.01
Diagnosis of pneumonia	466 (20.3)	2.32 [1.46–3.71]	1.45–3.73	0.0004
Diagnosis of cardiogenic pulmonary edema	186 (8.1)	2.33 [1.24–4.36]	1.22–4.32	0.008
Diagnosis of ARDS	64 (2.8)	5.57 [2.64–11.72]	2.64–11.64	< 0.001
Inotropic support on first day	962 (41.8)	2.53 [1.59–4.01]	1.56–4.03	< 0.001
Model 3: catheterized patients only (at least 24 h), n = 1,831				
Number of IPs occurred with catheter studied before 30 days: 69				
Weight < 80 kg	1,318 (72.0)	2.10 [1.09–4.0]1	1.05–3.9	0.03
Diagnosis of pneumonia	344 (18.8)	2.17 [1.32–3.57]	1.33–3.56	0.002
Diagnosis of cardiogenic pulmonary edema	152 (8.3)	2.60 [1.41–4.79]	1.42–4.67	0.002
Diagnosis of ARDS	55 (3.0)	5.66 [2.56–12.53]	2.54–12.5	< 0.001
Inotropic support on first day	945 (51.6)	1.82 [1.11–2.98]	1.11–2.99	0.02

* 95% confidence intervals (CIs) using bootstrap method provided nearly unbiased estimates of the CI of the β coefficients.

AIDS = acquired immunodeficiency syndrome; ARDS = acute respiratory distress syndrome; IP = iatrogenic pneumothorax.

invasive procedures remained a major cause of IP,[10] most notably central vein catheter insertion,[11,20] thoracentesis,[34] and bronchoscopy with transbronchial biopsy.[10]

Cumulative incidence curves showed a 3% risk of IP after 30 days. The risk was highest during the first 5 ICU days and decreased slightly thereafter. The occurrence of IP increased the duration of ICU and hospital stays. Moreover, using a case–control nested study with careful adjustment on severity at admission and duration of risk exposure, we demonstrated that IP was associated with a greater than twofold increase in the risk of death. In contrast to Chen *et al.*,[10] we observed that the increased risk of death was similar for IP-MV and for postprocedural IP. This result is in accordance with evaluations of mechanically ventilated patients,[9] patients with acute lung injury,[15] and patients with AIDS.[35] In one study involving a specific group of ARDS patients, IP-MV was not associated with an increased risk of death.[30] However, even in this study, mortality in patients with no air leak (39%) was not significantly lower than that in patients with IP-MV (46%). We also found a significant LOD score increase after IP. Moreover, IP was associated with cardiac arrest in 10 patients and occurred immediately before death in 10 other patients, supporting a major risk of death related to IP.

Table 3. Iatrogenic Pneumothorax Risk Score

	Pneumothorax Risk Score
1. Weight	
< 80 kg	1
> 80 kg	0
2. History of AIDS	
Yes	1
No	0
3. Diagnosis at ICU admission	
Diagnosis of cardiogenic pulmonary edema	1
Diagnosis of ARDS	2
Other diagnosis	0
4. Inotropic support on first day	
Yes	1
No	0
5. Central venous or pulmonary artery catheters on first day	
Yes	1
No	0
Total score	0–6 points

Points of the risk score are attributed in accordance to the estimated coefficients of each variable.

AIDS = acquired immunodeficiency syndrome; ARDS = acute respiratory distress syndrome; ICU = intensive care unit.

In our study, AIDS, body weight less than 80 kg, admission diagnosis of cardiogenic pulmonary edema or ARDS, insertion of a pulmonary artery or central venous catheter, and inotropic support on the first ICU day were independent risk factors for IP in ICU patients. Our findings are consistent with previous studies for ARDS[9,16] and lower body weight.[17,30] AIDS patients are often admitted for interstitial lung diseases or *Pneumocystis carinii* pneumonia,[35,36] which have been associated with a high risk of IP. Finally superior vena cava catheter insertion has been associated with a 0.5–3% risk of IP.[20]

Several limitations of our study should be discussed. First, symptomatic barotrauma without IPs was not recorded. This may have impacted the β estimates of the

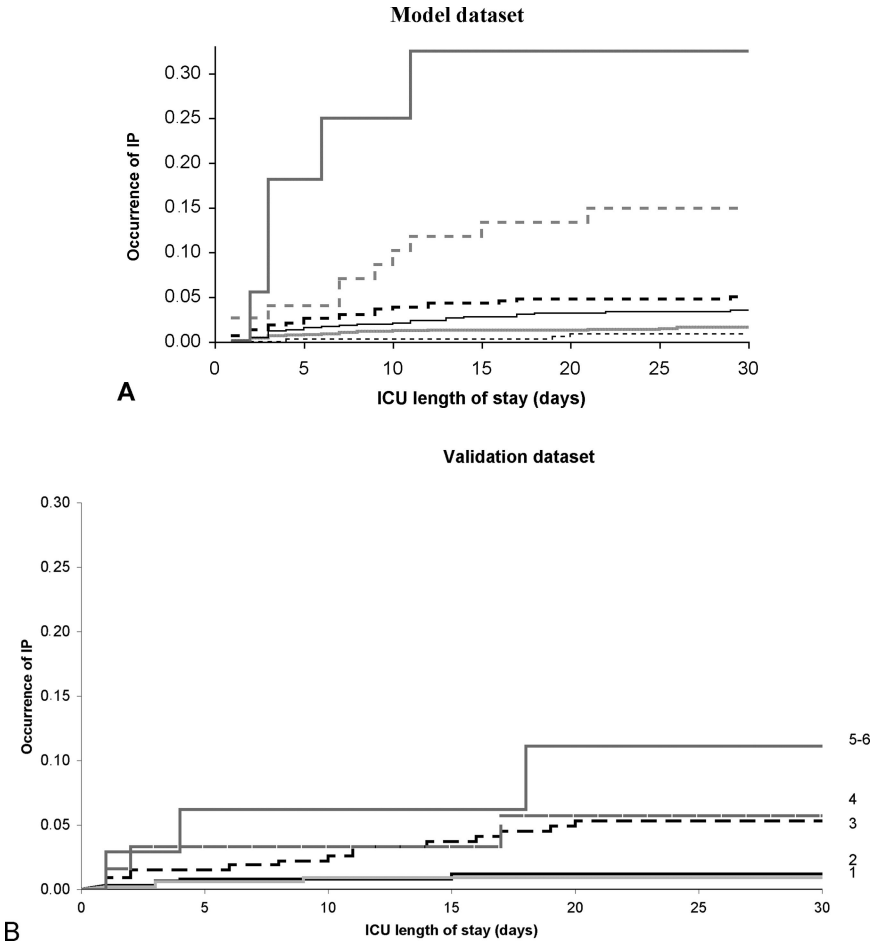

Fig. 3. Cumulative incidence of iatrogenic pneumothorax (IP) according to the level of the risk score in the model data set (*A*) and the validation data set (*B*). (See table 2 and the text for definition and calculation.) ICU = intensive care unit. Risk score of 0: model data set 3 IPs/374 patients, validation data set 0 IPs/272 patients; risk score of 1: model data set 23 IPs/1,506 patients, validation data set 8 IPs/611 patients; risk score of 2: model data set 27IPs/847 patients, validation data set 4 IPs/477 patients; risk score of 3: model data set 27 IPs/607 patients, validation data set 13 IPs/272 patients; risk score of 4: model data set 9 IPs/74 patients, validation data set 3 IPs/59 patients; risk score of 5 or 6: model data set 5 IPs/22 patients, validation data set 4 IPs/32 patients.

covariates and decreased the power of the study. In addition, because computed tomography was not performed routinely, the incidence of IP may have been underestimated. Also, because chest radiographs were not obtained routinely after death, cases of IP secondary to cardiac pumping during unsuccessful cardiac resuscitation procedures may have been missed. Second, the absence of plateau pressure and tidal volume in the database may have influenced the results of the risk factor evaluation and the IP risk score. However, plateau pressure was carefully maintained below 30 cm H_2O in all of the study ICUs. In this situation, plateau was not a risk factor for IP in two recent studies[9,30] Third, the relatively low number of IPs may have limited the power of the study for identifying risk factors. Finally, cardiogenic pulmonary edema was diagnosed by the investigators based on physical findings, echocardiography results, and the course. Pulmonary capillary pressure was not measured routinely. Therefore, the reproducibility of this variable is open to question.

We used our results to build an IP risk score that can be evaluated at ICU admission. The risk of experiencing IP within the first 30 days was less than 1% when the score was 0 and 15% when the score was 4. This risk score needs further external validation on another database. However, results obtained with a more recent data set of the OUTCOMEREA® database support the reliability of the IP risk score.

Iatrogenic pneumothorax should be a good quality indicator because it is clearly associated with ICU mortality. Requisites for valid comparisons of outcomes among ICUs include an accurate and comprehensive outcome measure, a sufficient sample size with unbiased sampling, and appropriate risk adjustment *via* application of a valid model to reliably collected data.[37] The IP risk score could be useful for comparing the IP rate across ICUs according to a specific level of risk. It could also be used to identify patients at high risk of IP, who would probably benefit from specific procedures for central venous catheter placement such as a careful risk–benefit estimation of central vein or pulmonary artery catheter insertion,[8] use of an insertion site that does not carry a risk of IP (femoral vessels), Doppler ultrasound guidance if subclavian or internal jugular vein insertion is required,[38] placement by an experienced physician,[11,17,20,39] and discontinuation of the procedure if the first two venipuncture attempts fail.[11]

Pneumothorax is one of the main iatrogenic events observed in ICU patients[1] and is relatively easy to diagnose. Our study confirms that IP is associated with sub-

Table 4. Characteristics of the Patients Included in the Case–Control Study

	Decedents (n = 745)	Survivors (n = 745)
At least one IP	39 (5%)	17 (2%)
Transfer from ward	401 (53.8%)	383 (51.4%)
Admission category		
Medical	536 (72%)	558 (75%)
Scheduled surgery	62 (8%)	89 (12%)
Unscheduled surgery	147 (20%)	98 (13%)
Admission diagnosis		
Pneumonia	186 (25%)	158 (21%)
Pulmonary edema	73 (10%)	67 (9%)
ARDS	19 (3%)	9 (1%)
Age	69 (56–77)	66 (52–74)
Weight		
< 50 kg	89 (12%)	47 (6%)
50–80 kg	506 (68%)	499 (67%)
≥ 80 kg	150 (20%)	199 (27%)
At least one chronic disease	468 (63%)	337 (45%)
AIDS	28 (4%)	26 (3%)
LOD	5 (3–7)	5 (3-7)
SAPS II	44 (36–55)	44 (36–55)
SOFA	6 (4–9)	6 (4–8)
Use during the first ICU day of		
Invasive mechanical ventilation	439 (59%)	470 (63%)
Inotropic support	301 (40%)	267 (36%)
Swan-Ganz, central venous catheter	312 (42%)	306 (41%)
ICU duration of stay	9 (5–16)	9 (5–16)

AIDS = acquired immunodeficiency syndrome; ARDS = acute respiratory distress syndrome; ICU = intensive care unit; IP = iatrogenic pneumothorax; LOD = Logistic Organ Dysfunction; SAPS = Simplified Acute Physiology Score; SOFA = Sequential Organ Failure Assessment.

sequent increases in ICU stay duration, resource use, and mortality. Interventions such as new ventilatory strategies for patients with ARDS,[9,40] improved experience of physicians with catheter insertion,[20] and use of ultrasound-located devices for central vein cannulation[38] reduce the rate of barotrauma. We suggest that the rate of IP could serve as an outcome measure in the ICU. Use of the IP risk score could allow reliable comparisons across groups, centers, or years.

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Appendix: List of Members of the OUTCOMEREA® Study Group

Scientific Committee

Jean-François Timsit, M.D., Ph.D., Staff Physician, ICU, Centre Hospitalier Universitaire Grenoble, France; Gilles Troché, M.D., Staff Physician, Hôpital A. Béclère, Clamart France; Pierre Moine, M.D., Ph.D., Staff Physician, Département d'Anesthesie-Réanimation, Hôpital Lariboisière, Paris, France; Arnaud de Lassence, M.D., Staff Physician, ICU, Hôpital Louis Mourier, Colombes, France; Élie Azoulay, M.D., Ph.D., Staff Physician, ICU, Hôpital Saint Louis, Paris, France; Yves Cohen, M.D., Professor, ICU, Hôpital Avicenne, Bobigny, France; Maïté Garrouste-Orgeas, M.D., Staff Physician, ICU, Hôpital Saint Joseph, Paris, France; Jean-Philippe Fosse, M.D., Staff Physician, ICU, Hôpital Avicenne, Bobigny, France; Lilia Soufir, M.D., Staff Physician, ICU, Hôpital Saint Joseph, Paris, France; Jean-Ralph Zahar, M.D., Attending Physician, Microbiology Department, Hôpital Necker, Paris, France; Christophe Adrie, M.D., Staff Physician, ICU, Hôpital de la Fontaine, Saint Denis, France; Jean Carlet, M.D., Staff Physician, ICU, Hôpital Saint Joseph, Paris, France; and François L'Hériteau, M.D., Attending Physician, ICU, Hôpital Bichat, Paris, France.

Biostatistical and Informatics Expertise

Sylvie Chevret, M.D. Ph.D., Professor, Medical Computer Sciences and Biostatistics Department, Hôpital Saint Louis, Paris, France; CorinneAlberti, M.D., Staff Physician, Medical Computer Sciences and Biostatistics Department, Hôpital Saint Louis, Paris, France; Frederik Lecorre, Informatician, Supelec, Gif sur Yvette, France; Didier Nakache, Informatic Engineer, Conservatoire National des Arts et Métiers, Paris, France; and Muriel Tafflet, Biostatistical Engineer, Outcomerea Organization, Rosny sous bois, France.

Investigators of the OUTCOMEREA® Database

Caroline Bornstain, M.D., Staff Physician, ICU, Hôpital Européen Georges Pompidou, Paris, France; Marie Thuong, M.D., Staff Physician, ICU, Hôpital de la Fontaine, Saint Denis, France; Marie-Alliette Costa de Beauregard, M.D., Staff Physician, Nephrology, Hôpital Tenon, Paris, France; Jean-Pierre Colin, M.D., Staff Physician, ICU, Hôpital de Dourdan, Dourdan, France; Eric Le Miere, M.D., Attending Physician, ICU, Hôpital Louis Mourier, Colombes, France; Antoine Caubel, M.D., Attending Physician, ICU, Hôpital Saint Joseph, Paris, France; William Marie, M.D., Attending Physician, ICU, Hôpital Saint Joseph, Paris, France; Christine Cheval, M.D., Staff Physician, SICU, Hôpital Saint Joseph, Paris, France; Eric Vantalon, M.D., Staff Physician, SICU, Hôpital Saint Joseph, Paris, France; Christophe Clec'h, M.D., Staff Physician, ICU, Hôpital Avicenne, Bobigny, France; François Vincent, M.D., Staff Physician, Nephrology, Hôpital Tenon, Paris, France; Amar Salah, M.D., Staff Physician, ICU, Hôpital Louis Mourier, Colombes, France; Laurent Montesino, M.D., Attending Physician, ICU, Hôpital Bichat, Paris, France; Etienne Pigné, M.D., Staff Physician, ICU, Hôpital Louis Mourier, Colombes, France; Alexandre Boyer, M.D., Staff Physician, ICU, Hôpital Pellegrin, Bordeaux, France; Olivier Tuil, M.D., Staff Physician, ICU, Hôpital Avicenne, Bobigny, France; Bruno Mourvillier, M.D., Staff Physician, ICU, Hôpital d'Aulnay sous bois, France; Samir Jamali, M.D., Staff Physician, ICU, Hôpital de Dourdan, Dourdan, France; Delphine Moreau, M.D., Staff Physician, ICU, Hôpital Saint Louis, Paris, France; Guillaume Thiery, M.D., Staff Physician, ICU, Hôpital Saint Louis, Paris, France; Alexandre Duguet, M.D., Attending Physician, Hôpital Pitié-Salpétriere, Paris, France; Christian Laplace, M.D., Attending Physician, ICU, Hôpital Kremlin-Bicêtre, Bicêtre, France; and Thierry Lazard, M.D., Staff Physician, ICU, Hôpital de la Croix St Simon, Paris, France.