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Increased use of noninvasive ventilation in French intensive care units

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Abstract *Objectives:* A prospective survey of French intensive care units (ICUs) in 1997 showed moderate and variable use of noninvasive ventilation (NIV). This study examined changes in NIV use in French ICUs after the intervening 5 years. *Settings:* Patients were enrolled in a prospective survey in 70 French ICUs. *Methods:* Three-week survey, with prospective inclusion of all patients requiring ventilatory support. *Measurements and results:* Overall 1,076 patients received ventilatory support (55% of admissions). First-line NIV was significantly more common than 5 years earlier, overall (23% vs. 16%) and especially in patients not intubated before ICU admission (52% vs. 35%). Reasons for respiratory failure were coma (33%), cardiogenic pulmonary edema (8%), acute-on-chronic respiratory failure (17%), and de novo respiratory failure (41%). Significant

increases in NIV use were noted for acute-on-chronic respiratory failure (64% vs. 50%) and de novo respiratory failure (22% vs. 14%). Among patients given NIV, 38% subsequently required endotracheal intubation (not significantly different). Independent risk factors for NIV failure were high SAPS II and de novo respiratory failure, whereas factors associated with success were good NIV tolerance and high body mass index. *Conclusions:* NIV use has significantly increased in French ICUs during the past 5 years, and the success rate has remained unchanged. In patients not previously intubated, NIV is the leading first-line ventilation modality. The proportion of patients successfully treated with NIV increased significantly over the 5-year period (13% vs. 9% of all patients receiving ventilatory support).

Keywords Acute respiratory failure · Cardiogenic pulmonary edema · Chronic obstructive pulmonary disease · Pneumonia · Endotracheal intubation

Introduction

Noninvasive ventilation (NIV) offers major benefits in selected patients with acute respiratory failure requiring intensive care unit (ICU) admission. NIV was introduced for critically ill patients in the 1990s when randomized

controlled trials showed that NIV reduced the risk for endotracheal intubation (ETI) in patients with acute on chronic respiratory failure [1, 2, 3]. A similar effect was then found in patients with cardiogenic pulmonary edema [4] or hypoxemic respiratory failure [5]. To determine whether the benefits observed in clinical trials

occurred also in everyday practice we evaluated NIV use in 1997 in 42 French ICUs [6]. We included all patients requiring ventilatory support for acute respiratory failure. The results showed that NIV was used in 16% of patients overall and in 35% of patients without ETI at admission. NIV success significantly decreased the risk of pneumonia and death. Since 1997 several studies have further documented the benefits of NIV and have expanded the indications for NIV to patients with various forms of hypoxemic respiratory failure [5, 7], immunosuppression [8, 9, 10, 11], and specific postoperative conditions [12]. NIV was found superior over conventional oxygen therapy in patients with cardiogenic pulmonary edema [13] and benefited patients with acute-on-chronic respiratory failure in various situations [14, 15, 16, 17]. Finally, the use of NIV in acute respiratory failure was discussed at an international consensus conference [18].

To determine whether changes have occurred in the use of NIV we repeated another prospective multicenter survey in 2002, 5 years after the initial survey. We compared the results to those of the earlier survey. This study has been presented in abstract form [19].

Methods

Study centers

A prospective observational study was conducted in French ICUs. In the name of a task force on mechanical ventilation we contacted the 376 ICUs whose directors were members of the French Society for Intensive Care (Société de Réanimation de Langue Française, SRLF); participation was on a voluntary basis, and we specified that we were equally interested by centers performing or not performing NIV; 102 ICU directors initially agreed to participate.

Patients

We included all patients admitted between 4 and 24 March 2002 who required endotracheal or noninvasive ventilation for acute respiratory failure at any time during the ICU stay. The total number of admissions during the study period was recorded. In each ICU the study investigators included each patient prospectively and completed a standardized form supplying data from admission to ICU discharge or death in patients receiving ventilatory support. Completed forms were mailed to the coordinating study center at the end of the 3-week study period or when the last included patient had died or been discharged from the ICU, whichever occurred first.

Data on demographics and history consisted of age, gender, and location before hospital and ICU admission. The Simplified Acute Physiology Score (SAPS) II [20] was used to assess severity of illness and the Logistic Or-

gan Dysfunction (LOD) score to evaluate organ dysfunction [21] at admission. Underlying diseases were scored 0 if not present or not fatal, 1 if expected to cause death within 5 years, and 2 if expected to cause death within 1 year [22]. Previous ICU stays, previous experience with ventilatory assistance, and history of home oxygen therapy were recorded, as well as history of chronic pulmonary disease (COPD) and other causes of chronic respiratory failure, chronic heart failure (NYHA III or IV), and cancer or immunosuppression (defined as neutropenia below $1000/\text{mm}^3$ after bone marrow transplantation or anticancer chemotherapy, immunosuppressive therapy for solid organ transplantation, corticosteroid therapy of 20 mg or more per day for at least 3 weeks, or AIDS). Immediately before initiating ventilatory assistance the followings were recorded: reason for respiratory failure, arterial blood gas values, respiratory rate, heart rate and systolic arterial blood pressure, ability of the patient to mobilize secretions (yes, 1; and no, 2); Glasgow Coma Scale score; severity of encephalopathy scored from 0–4 (0, no abnormalities; 1, hypertonia or cogwheel rigidity with normal consciousness; 2, tremor, asterixis, or sleepiness; 3, confusion or agitation; and 4, prostration or obtundation), and body temperature. The characteristics of noninvasive ventilatory support were recorded throughout the first week or until ETI was required, as well as the patient-to-nurse ratio, type of ventilator (ICU type, NIV ventilator defined as a ventilator that has been designed for the specific purpose of in-hospital NIV, and home device defined as a ventilator designed primarily for home ventilation), mode of ventilation, main ventilator settings, type of mask (facial, nasal, integral mask or helmet), airway humidification system (heat-moisture exchanger, heated humidifier, no humidification device), use of nasal protection (local nasal skin protection with a hydrocolloid gel that prevents the occurrence of skin irritation and breakdown), and arterial blood gas values on the first ventilation day. We also recorded: clinical tolerance by the patient (from 1, very good to 4, bad) assessed by the clinician, extent of air leaks during NIV (from 1, very small or none to 5, massive), side effects of NIV, reasons for discontinuing NIV, and whether ETI was performed subsequently.

Data quality

All patient forms were reviewed by the principal investigator (A.D.) for compliance with inclusion criteria, correct calculation of severity and organ failure scores, and completeness and accuracy of daily data recording. Investigators were contacted about suspected errors or missing data. A double data entry procedure was used, with a system that automatically alerted keyboarding personnel to aberrant, outlier, or contradictory values. Data that triggered the alert system or showed discrepancies were checked and corrected.

A comparison was performed with the survey performed in 1997 in 42 French ICUs [6]. Of note, more centers were included in this survey; only 28 centers participated in both surveys, and the 1997 survey also included one center each from Spain, Switzerland, Belgium, and Tunisia.

Statistical analysis

The median and the interquartile range were calculated for continuous variables and the absolute and relative frequencies for categorical variables, as well as the 95% confidence intervals (95%CI) where appropriate. Each potential risk factor for NIV failure was evaluated in a univariate model; for continuous data, we used the Student's *t* test or the Mann-Whitney *U* test as appropriate and for categorical variables the χ^2 test or Fisher's exact test. Factors yielding *p* values of 0.05 or less were entered into a logistic regression model, except those redundant with other factors (NIV during the first 24 h with NIV tolerance and LOD score with SAPS II) or having a high missing value rate (Glasgow Coma Scale score). Goodness-of-fit was assessed using the Hosmer-Lemeshow χ^2 test and discrimination using the area under the receiver operating characteristic (ROC) curve. Accuracy was considered good when the area under the ROC curve ranged from 0.70–0.80 and excellent when it was greater than 0.80. Continuous variables were introduced either without correction or after dichotomization according to the median value. The adjusted odds ratio and 95% confidence interval were calculated for each factor that was significant in the logistic regression model. Differences with *p* values less than 0.05 were considered statistically significant. All tests were two-tailed. Statistical tests were performed using Intercooled STATA 8.2 software (StatCorp, Texas, USA).

Results

ICUs

Complete data were obtained for 70 ICUs, including 38 (54%) in nonuniversity hospitals and 32 (46%) in university hospitals. There were 24 (34%) medical ICUs, 42 (60%) medical-surgical ICUs, and 4 respiratory ICUs. These 70 ICUs had medians of 11 beds (interquartile range, IQR, 8–14), declared having 458 admissions per year (IQR, 350–618) and 52% of patients requiring mechanical ventilation (IQR, 40–61). Among the 70 participating units, 34 had used NIV in more than 50 patients during the year preceding the survey, 31 centers used NIV in 10–50 patients, and only 1 center reported using NIV in 1–10 patients (4 missing data). No unit declared not using NIV.

Demographics

Of the 1943 patients admitted during the 3-week study period 1,076 (55%; 95%CI, 53–58) required mechanical ventilation, as compared to 51% (95%CI, 49–54) in 1997 (*p* = 0.03). Figure 1 shows the distribution of patients treated with NIV and with ETI. Overall NIV was the first-line ventilation modality in 249 (23%) of 1,076 patients (95%CI, 21–26), a significant increase compared to 1997 (16%, 95%CI, 13–19, *p* < 0.0001; Fig. 2). NIV use in patients admitted to the ICU without ETI was also significantly increased compared to 1997 (52%; 95%CI, 46–58; vs. 35%; 95%CI, 30–41; *p* < 0.0001; Fig. 2). Variations in NIV use among the ICUs of the study are shown on Fig. 3. In 2002 33 patients received NIV before ICU admission, compared to none in 1997. In the 28 centers that participated in both surveys 498 patients were ventilated and the rate of NIV use in 2002 was 34%.

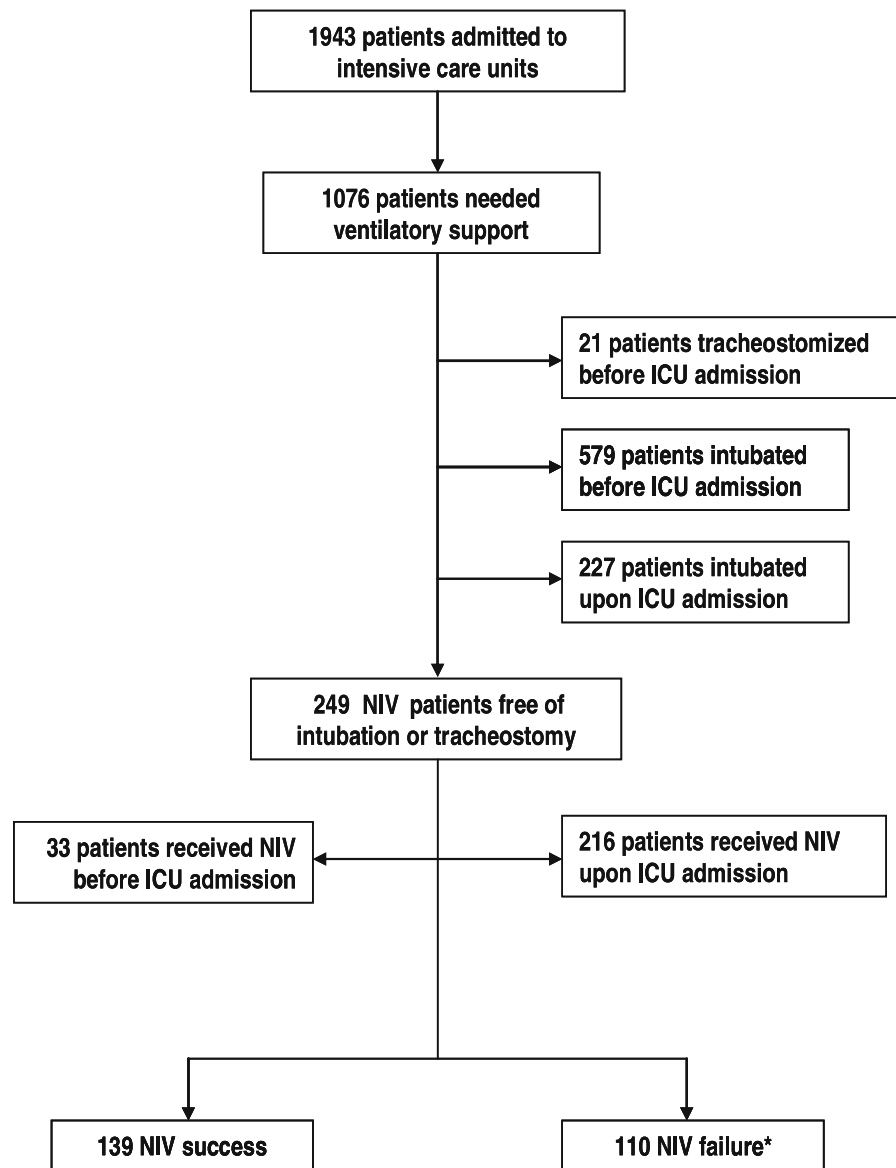
The causes of acute respiratory failure were classified into four groups: 172 (16%) patients had acute-on-chronic respiratory failure, including 11% with obstructive disease and 4.5% with restrictive disease; 366 (34%) patients had coma of various causes (e.g., stroke, severe drug overdose) resulting in ventilatory failure as the main reason for the need of ventilatory support: in this group, intubation was performed to protect upper airways and allow achievement of satisfactory gas exchanges through mechanical ventilation; patients with coma secondary to respiratory acidosis were classified in the previous group; 86 (8%) patients had cardiogenic pulmonary edema; and 452 (42%) patients had de novo respiratory failure, including postoperative failure (14%), pneumonia (13%), extrapulmonary sepsis (6%) and others. NIV was used in one patient with coma. Compared with 1997, NIV use increased significantly for acute-on-chronic respiratory failure (64%, 95%CI, 56–71, vs. 50%, 95%CI, 40–60; *p* = 0.03) and for de novo respiratory failure (22%, 95%CI, 19–26 vs. 14%, 95%CI, 10–18; *p* = 0.003) (Fig. 4). In the 28 centers that participated in both surveys, the use of NIV in 2004 was comparable, 69% for acute-on-chronic respiratory failure, 29% for de novo respiratory failure, and 52% for cardiogenic pulmonary edema.

Among the 172 patients who received ventilatory support for an acute-on-chronic respiratory failure, 24% were intubated outside the ICU, 64% received NIV, and only 12% were intubated (as a first line treatment) in the ICU. Among those, 60% had a severe ventilatory acidosis (pH < 7.20), 60% had an extrapulmonary organ failure, and 60% had a severe encephalopathy.

NIV characteristics

Pressure support was the most widely used ventilatory mode (83%). Assist-control ventilation was used in 7% of patients and spontaneous breathing with continuous

Fig. 1 Distribution of patients according to the mode of ventilatory assistance. *NIV* Noninvasive ventilation. *In the text 109 *NIV* failures are considered after exclusion of one patient with coma



positive airway pressure in 8%. An ICU-type ventilator was used in 79% of cases, an NIV ventilator in 12%, and a home device in 5% (4% missing data). Airway humidification was achieved using a heat-moisture exchanger in 48% of patients and a heated humidifier in 19%; no humidification device was used in 30% of patients. NIV was delivered via a face mask in 83% of patients, a total face mask (but no helmet) in 9%, and a nasal mask in 6%. A nasal protection was used in 45% of the patients ventilated through a face mask.

Response to NIV

For the effectiveness analysis we excluded the single patient with coma who was given NIV as this patient was

switched to ETI upon evaluation by the senior physician, whose decision was independent of the effect of NIV and based on the need to protect the airway. Of the 248 remaining patients 117 (47%) had an early discontinuation of NIV, i.e., while continued indications for ventilatory assistance were present. Reasons for discontinuation were inadequate efficacy [59%, with absence of clinical improvement (22%), lack of arterial blood gas improvement (6%), or both (31%)], full dependence on ventilatory support contrasting with the need to interrupt NIV (26%), inability to manage copious secretions (14%), agitation (13%), intercurrent event (12%), and patient refusal (8%) (some patients had more than one reason). The premature NIV discontinuation rate was similar to that seen in 1997 (47% vs. 48%, respectively), but significant differences were found regarding reasons for discontinuation: de-

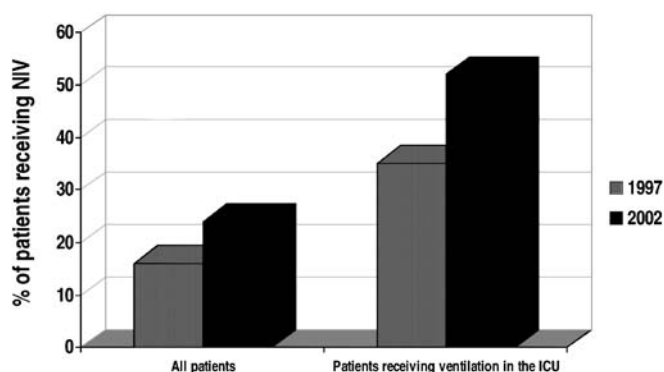


Fig. 2 Change in the use of noninvasive ventilation between 1997 and 2002 in all patients requiring mechanical ventilation and in patients started on ventilation in the ICU. * $p < 0.05$ between the two studies

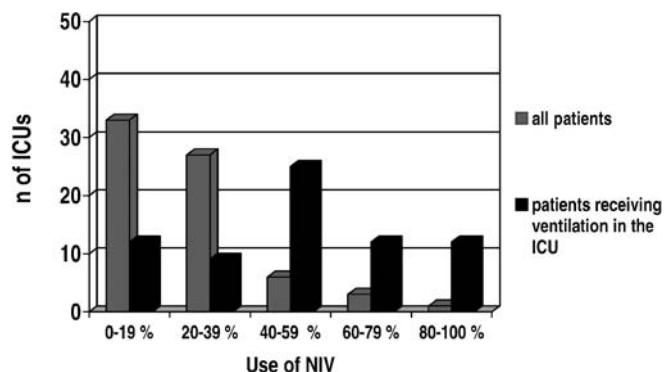


Fig. 3 Variation in noninvasive ventilation use among intensive care units in the 2002 survey, as a percentage of all patients requiring mechanical ventilation and as a percentage of patients started on ventilation in the ICU

creases were seen for inadequate efficacy (from 84% to 59%), inability to manage copious secretions (from 32% to 14%), and patient refusal (from 22% to 8%); whereas a significant increase was noted for full dependence (from 14% to 26%). Of the 117 patients with premature NIV discontinuation 94 (80%, representing 38% of all NIV patients) received ETI, and 15 died within 24 h following NIV discontinuation without receiving ETI because of do-not-intubate orders. These 109 patients were classified as NIV failures. The 8 patients with premature NIV discontinuation who survived without receiving ETI and the 131 patients treated with NIV until they no longer required assistance were classified as NIV successes. This 56% success rate (95%CI, 50–62) was similar to the rate in 1997 (60%, 95%CI, 50–69), using the same definition. Due to the increased use of NIV, the proportion of patients successfully treated by NIV in the overall population requiring mechanical ventilation was higher in the present

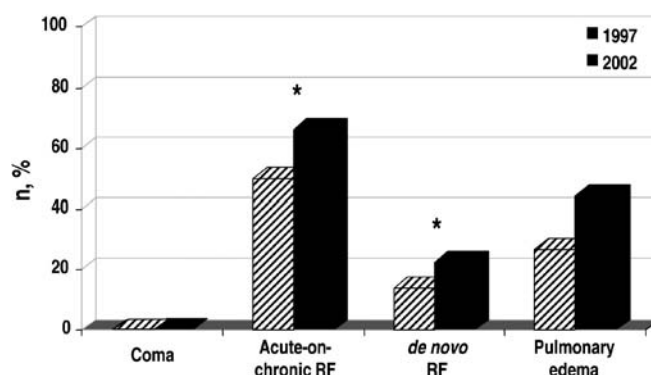


Fig. 4 Changes in relative use of noninvasive ventilation between 1997 and 2002, according to the reason for respiratory failure (RF). * $p < 0.05$ between the two studies

study than in 1997 (13%, 95%CI 11–15; vs. 9%, 95%CI 7–12; $p = 0.03$).

Table 1 Factors associated with failure of noninvasive ventilation in the univariate analysis; values are medians (parentheses interquartile range) unless otherwise indicated

	NIV failure ($n = 109$)	NIV success ($n = 139$)	p
SAPS II, points	43 (36–53)	34 (27–38)	<0.0001
LOD score, points	4 (3–7)	2 (1–4)	<0.0001
De novo ARF, n (%)	60 (55)	41 (29)	<0.0001
Glasgow Coma Scale ^a	14 (12–15)	15 (14–15)	0.001
Immunosuppression	25 (23)	15 (11)	0.01
Systolic arterial pressure ≤ 130 mmHg	63 (60)	60 (48)	0.06
Respiratory rate ≥ 35 bpm	37 (36)	24 (20)	0.008
PaO ₂ /FIO ₂ ≤ 200 mmHg	50 (54)	44 (40)	0.05
Body mass index	24 (21–28)	26 (22–31)	0.006
Time with NIV during the first 24 h (h)	6 (2–11)	8 (5–12)	0.007
Good NIV tolerance	15 (7%)	53 (39%)	<0.0001
NIV with high level of leaks	73 (69%)	68 (50%)	0.003
NIV in patients with do-not-intubate orders	17 (16%)	16 (12%)	0.35

^a 23 patients had missing values for the Glasgow Coma Scale (8/15)

Abbreviations: ARF acute respiratory failure, LOD logistic organic dysfunction, NIV noninvasive ventilation, SAPS Simplified Acute Physiology Score

Table 2 Independent risk factors for failure of noninvasive ventilation identified by multivariate analysis; Hosmer-Lemeshow $\chi^2 = 7.50$, $p = 0.48$; area under the receiver operating characteristics curve = 0.81

	Adjusted odds ratio	95% confidence interval	p
SAPS II ^a	1.07	1.03–1.10	<0.0001
Good NIV tolerance ^a	0.38	0.15–0.93	0.03
De novo ARF ^a	2.17	1.01–4.67	0.04
Body mass index ^a	0.94	0.89–0.99	0.04
NIV with high level of leaks	1.63	0.77–3.42	0.20
PaO ₂ /FIO ₂ ≤ 200 mmHg	1.29	0.60–2.78	0.14
Respiratory rate ≥ 35 bpm	1.32	0.54–3.19	0.54
Immunosuppression	0.89	0.33–2.41	0.82

^a Parameters significantly associated with result of NIV
Abbreviations: ARF acute respiratory failure, NIV noninvasive ventilation, SAPS Simplified Acute Physiology Score

Predictors of successful NIV

Table 1 reports the main characteristics in the groups with successful NIV and failed NIV. The patient with coma who received NIV, was excluded from this analysis. Severity of illness, reasons for acute respiratory failure, preexisting immunosuppression, and several physiological characteristics at NIV initiation, including PaO₂/FIO₂ were significantly different between the two groups. NIV outcome was not influenced by the type of ventilation (i.e., type of ventilator, humidification device, PEEP or pressure support level), neither by the patient to nurse ratio. The scores for air leaks and NIV tolerance were significantly different between the two groups.

As shown in Table 2, a high SAPS II score and de novo respiratory failure were the two independent factors associated with failed NIV. Good NIV tolerance score and high body mass index were independently associated with successful NIV. The same analysis was conducted separately in patients with de novo respiratory failure [risk factors were SAPS II, odds ratio (OR) 1.05, CI 1.01–1.09, $p = 0.007$ and NIV leaks, OR 2.63, CI 1.03–6.71, $p = 0.044$], and patients with acute-on-chronic respiratory failure or cardiogenic pulmonary edema (risk factors were SAPS II, OR 1.07, CI 1.03–1.10, $p < 0.0001$ and good NIV tolerance, OR 0.30, CI 0.11–0.77, $p = 0.012$).

Discussion

Increased NIV use

NIV use increased from 16% to 24% in all ICU patients requiring ventilatory support for acute respiratory failure and from 35% to 52% in those without ETI before or at ICU admission. A retrospective, observational, cohort study showed a steady rise in NIV use from 1994–2001 in

a single ICU in France [23]. The present results suggest a similar trend in French ICUs.

Before discussing the results, some limitations of the present study warrant mentioning. The present survey was conducted in 2002, and it may not even reflect present-day practices since further changes may have occurred before publication of the results. Also, this 2002 survey may have underestimated the use of NIV since patients in whom NIV was entirely performed into the emergency room or in the ward were not included in the survey. Another limitation is the fact that it was conducted in only a single country. To evaluate the course of NIV use over years, however, we wished to compare the use of NIV in the present study with the use of NIV in a precedent survey conducted in France. Only a part of French ICUs participated in this survey, which could have introduced a bias, physician being more likely to participate if they were “NIV believer.” When intensivists were asked to participate, we clearly specified that we were similarly interested if they use or did not use NIV. Finally, the centers that participated in the two surveys were not exactly the same, as indicated in the methods section, but 28 centers that were part of the 1997 survey participated in the 2002 survey. The NIV use and its increase between the two surveys among the centers that participated in the two surveys were comparable to what was observed overall. We increased the number of centers to make it more representatives of French ICUs with more nonuniversity centers.

That NIV has gained ground so rapidly is remarkable, as many medical advances have been slow to take root in clinical practice. Although it differs in many aspects, the example of the tidal volume range in acute lung injury does not seem to offer the example of such a rapid change in practice. Weinert et al. [24] investigated trends in ventilatory assistance in 398 patients with acute lung injury treated in three teaching hospitals between 1994 and 2001 and found that mean prescribed tidal volume was still 10.1 ± 1.9 ml/kg actual body weight in the 2 years following the release of the NIH study, in which 6 ml/kg predicted body weight was superior over 12 ml/kg. Our survey was not designed to identify the reasons for increased NIV use. Nevertheless, the above example suggests that the accumulation of data on benefits from NIV may not be the only reason. The factors that govern acceptance of new treatments by physicians in everyday practice have been investigated [25, 26], and the trigger that motivates a change in prescription practices has emerged as more powerful than exposure to new information [26]. In a study evaluating the NIH Consensus Development Program [27] Kanouse and Jacoby [26] suggested that a motivating trigger could be the belief by the physician that “his or her patients are not experiencing a satisfactory outcome.” Intensivists have noted poor outcomes in patients intubated for acute-on-chronic obstructive respiratory failure, most notably prolonged need for mechanical ventilation and difficulties during the weaning process.

This clinical reality may have prompted a readiness for change among intensivists. Greco and Eisenberg [25] also suggested that physicians change their practice only when they perceive the change as beneficial to their patients. Thus the major and readily perceptible benefits of NIV may explain the rapid growth of NIV use documented in the present study. Other factors may facilitate rapid adoption of NIV: the resources needed for NIV are under the control of the physician; NIV failure leads to ETI, which is simply the standard treatment [26]. Furthermore, giving physicians information about their practices may influence their readiness to adopt changes [25]. The 1997 survey provided information on practices regarding NIV. Finally, the 1999 consensus conference may have played a role [18]. The impact of consensus conferences on medical practices is controversial [28] and may be limited in some cases [29]; nevertheless, consensus conferences may hold potential for improving medical practices [30].

NIV failure

Despite this large increase in NIV use the failure rate remained unchanged between 1997 and 2002. This steady failure rate was not associated with a major increase in the severity of patients receiving NIV, and the SAPS II of patients treated with NIV was comparable between the two surveys (39 ± 16 in the present survey vs. 36 ± 20 in 1997). In our univariate analysis several variables differed between the success and failure groups. Many of these variables have been shown to predict NIV failure, such as level of consciousness [6, 31], $\text{PaO}_2/\text{FIO}_2$ [32], presence of leaks [33], and NIV tolerance score [6]. The univariate analysis found that immunosuppression was associated with a higher rate of NIV failure, but this did not remain in the multivariate analysis. NIV has been found beneficial in immunosuppressed patients [8, 10, 11]. The univariate analysis also found that do-not-intubate orders did not differ between the success and failure groups. This result is consistent with those of previous studies that found NIV success rates averaging 60% in these patients [34, 35]. Nevertheless, the present survey did not assess the long-term prognosis of these patients. The present study identified four independent factors, namely, worse SAPS II, de novo respiratory failure, low body mass index, and poor NIV tolerance. A worse SAPS II or severity score was associated with NIV failure in other studies [32, 36] including our 1997 survey [6]. NIV use in patients with de novo respiratory failure was initially controversial until recent trials [5, 8, 37]. We observed a high rate of NIV failure leading to ETI in patients with de novo respiratory failure (54%). Pneumonia was the leading cause of hypoxemia in patients requiring ETI, and similar or higher rates of NIV failure have been reported in patients with pneumonia [5, 38, 39, 40]. This survey also indirectly suggests that most of the patients treated with NIV in this

survey needed ventilatory support. Indeed, among the 117 patients in whom NIV was discontinued prematurely only 8 survived without further ventilatory support. Therefore our results should not be construed as evidence that NIV is not beneficial in patients with de novo respiratory failure; instead, they suggest that physicians should be aware of the high risk of failure in this patient subgroup.

Good NIV tolerance, as assessed using a semiquantitative score, independently predicted success. This score, however, does not allow identification of a specific reason for poor NIV tolerance, which can be related to patient, equipment, or settings. The outcome of NIV seemed independent of the mode of ventilation, type of ventilator, and humidification device. This result should be interpreted with caution, as the study was probably not adequately powered to detect a role for each of these factors. Although of marginal significance, a high body mass index was associated with successful NIV. Because the median value was 25 kg/m^2 , this result does not indicate a protective effect of obesity. Among the possible explanations, a higher rate of upper airway obstruction responsive to mask positive pressure ventilation or a different level of nutrition could play a role [36].

Among the patients who received ventilatory support for an acute-on-chronic respiratory failure, 24% were intubated outside the ICU, and 12% were intubated as a first line treatment in the ICU. Among those, 60% had a severe ventilatory acidosis ($\text{pH} < 7.20$), 60% had an extrapulmonary organ failure, and 60% had severe encephalopathy. Some of these patients might possibly have been intubated because of insufficient familiarity with the technique, but a majority were probably considered as having contraindication to the technique, namely an organ failure other than respiratory or an encephalopathy that was considered too severe to allow the technique to be initiated.

In conclusion, compared to 1997, NIV use has significantly increased in French ICUs, up to 24% overall and 52% of patients admitted without ETI. The number of patients successfully treated by NIV among all patients requiring mechanical ventilation was higher in the present study. Future efforts should focus on improving patient selection and on enhancing patient acceptance via better adjustment of NIV settings [33, 41, 42].

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