Noninvasive versus invasive ventilation for acute respiratory failure in patients with hematologic malignancies: A 5-year multicenter observational survey

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Background: **Mortality is high among patients with hematologic malignancies admitted to intensive care units for acute respiratory failure. Early noninvasive mechanical ventilation seems to improve outcomes.**

Objective: **To characterize noninvasive mechanical ventilation use in Italian intensive care units for acute respiratory failure patients with hematologic malignancies and its impact on outcomes vs. invasive mechanical ventilation.**

Design, Setting, Participants: **Retrospective analysis of observational data prospectively collected in 2002–2006 on 1,302 patients with hematologic malignancies admitted with acute respiratory failure to 158 Italian intensive care units.**

Measurements: **Mortality (intensive care unit and hospital) was assessed in patients treated initially with noninvasive mechanical ventilation vs. invasive mechanical ventilation and in those treated with invasive mechanical ventilation *ab initio* vs. after noninvasive mechanical ventilation failure. Findings were adjusted for propensity scores reflecting the probability of initial treatment with noninvasive mechanical ventilation.**

Results: **Few patients (21%) initially received noninvasive mechanical ventilation; 46% of these later required invasive mechanical ventilation. Better outcomes were associated with successful noninvasive mechanical ventilation (vs. invasive mechanical ventilation *ab initio* and vs. invasive mechanical ventilation after noninvasive mechanical ventilation failure), particularly in patients with acute lung injury/adult respiratory distress syndrome (mortality: 42% vs. 69% and 77%, respectively). Delayed vs. immediate invasive mechanical ventilation was associated with slightly but not significantly higher hospital mortality (65% vs. 58%, $p = .12$). After propensity-score adjustment, noninvasive mechanical ventilation was associated with significantly lower mortality than invasive mechanical ventilation.**

Limitations: **The population could not be stratified according to specific hematologic diagnoses. Furthermore, the study was observational, and treatment groups may have included unaccounted for differences in covariates although the risk of this bias was minimized with propensity score regression adjustment.**

Conclusions: **In patients with hematologic malignancies, acute respiratory failure should probably be managed initially with noninvasive mechanical ventilation. Further study is needed to determine whether immediate invasive mechanical ventilation might offer some benefits for those with acute lung injury/adult respiratory distress syndrome. (Crit Care Med 2011; 39:000–000)**

Key Words: acute respiratory failure; invasive mechanical ventilation; mortality; noninvasive mechanical ventilation

High mortality rates among intensive care unit (ICU) patients with underlying hematologic malignancies (1) have been linked to various factors (2–4), including the aggressive, frequently invasive treatments that characterize today's ICUs. This approach facilitates the development of severe infections and multiple-organ failure, events that are already common in patients with immunodeficiency (e.g., neutropenia, deficits in cell-mediated or humoral immunity) and exposure to chemotherapy (5–10). Consequently, older recommendations discouraged the use of invasive approaches in patients with hematologic malignancies (11, 12). Recent progress in the fields of oncology and intensive care has substantially reduced ICU-related mortality among these patients (13). Acute respiratory failure (ARF) is the most common form of organ failure in this population and a major predictor of mortality (14). Early management with noninvasive mechanical ventilation (NIMV) seems to improve outcomes (15–18) and may even eliminate the need for ICU admission. Less is known about the impact of decisions to use NIMV after ICU admission. We set out to characterize the use of NIMV in Italian ICUs for ARF patients with hematologic malignancies and to determine the impact on outcomes of this approach vs. conventional invasive mechanical ventilation (IMV).

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MATERIALS AND METHODS

Data Collection and Patients

This study was approved by the review board of the Mario Negri Institute for Pharmacologic Research. It involved retrospective analysis of exclusively observational data from the Italian Group for the Evaluation of Interventions in Intensive Care Medicine (GIVITI) Project Margherita database (19, 20) that had been prospectively collected from 2002 through 2006 in 158 ICUs throughout Italy. A complete list of study participants appears in the appendix. These units routinely document each ICU admission on a standardized electronic form that includes conditions present at ICU admission; Simplified Acute Physiology Score II (SAPS-II) variables (21); conditions that develop and major procedures performed during the ICU stay; length and outcomes (vital status) of the ICU and total hospital stays; and, since 2005, infections present at or after ICU admission. Recorded information reflects the care actually delivered in the units, all of which adhere in principle to internationally accepted consensus guidelines regarding the diagnosis and classification of infections (22, 23), acute lung injury (ALI), acute respiratory distress syndrome (ARDS) (24), multiple-organ failures (25), and the use of NIMV vs. IMV (26). All units were equipped with ICU ventilators and equipment for delivering NIMV.

The cases we analyzed met the following criteria: 1) ICU admission date 2002–2006; 2) ARF at ICU admission; 3) hematologic malignancy (acute or chronic myelogenous leukemia, acute or chronic lymphocytic leukemia, polycythemia vera, Hodgkin's disease, lymphosarcoma, Waldenstrom's macroglobulinemia, myeloma, other lymphomas) as the hospital admission diagnosis or a comorbidity; 4) no previous bone marrow transplantation; 5) length of ICU stay >24 hrs; and 6) no surgery on the day of ICU admission. In each ICU, cases were selected by a trained physician with telephone access to project coordinators. The form provided detailed descriptions of each item, and each entry was automatically analyzed for inherent and relative inconsistency (e.g., incorrect dates, mechanical ventilation without respiratory failure). Inconsistent entries were reviewed by project coordinators and corrected when possible. To reduce selection bias, we excluded patients admitted during months in which over 10% of the admissions in the same unit had incomplete data series.

Upon arrival in the ICU, each patient was placed on IMV (oro- or nasotracheal intubation, continuous pressure- or volume-controlled ventilation) or NIMV (administered via face mask or helmet using the pressure-support model [27, 28]). The choice was based exclusively on the clinical judgment of the physician on duty when the patient arrived, although the principles underlying these decisions were identical in all units (26, 28). NIMV was delivered continuously for the first 24 hrs and as needed thereafter (16, 17). Patients were closely monitored and promptly switched to IMV if they presented any of the following: PaO_2/F_{IO_2} ratio <150 (after >1 hr of treatment); PaO_2 consistently <65 mm Hg with an F_{IO_2} >0.6; persistent dyspnea, tachypnea, accessory muscle use; conditions requiring intubation for airway protection (e.g., coma, seizures) or secretion management; hemodynamic or electrocardiographic instability (e.g., systemic hypotension lasting >1 hr despite fluid resuscitation); or intolerance of the NIMV interface (16, 21, 26).

Statistical Analysis

Data were analyzed with SAS software (version 9.02, SAS, Cary, NC). Results were expressed as proportions for categorical and ordinal variables, medians and interquartile ranges for ordinal and continuous variables, and mean with standard deviation (SD) for continuous variables; 95% test-based confidence intervals (CIs) were computed for each estimate.

Our analysis included three between-group comparisons: 1) cases managed *ab initio* with IMV vs. those initially managed with NIMV (to identify the potential impact of this decision on outcome); 2) patients successfully and unsuccessfully treated with NIMV (to identify possible risk factors for NIMV failure); and 3) patients who received IMV *ab initio* and after NIMV failure (to identify the potential impact on outcome of unsuccessful NIMV trials). Intergroup differences were assessed with the Cochran-Mantel-Haenszel chi-square test (for qualitative variables) and with the *t* test or Wilcoxon's test (as appropriate for quantitative variables).

To minimize bias related to the nonrandom treatment group allocation of patients, we adopted a regression adjustment scheme involving individual propensity scores (29) reflecting the probability of initial prescription of NIMV (as opposed to IMV) based on baseline patient characteristics. The score was based on a logistic regression model that included all available demographic and clinical variables as covariates (see online supplement). Centers that never used NIMV were excluded from this model to avoid biases in identifying the criteria actually used by ICU physicians in choosing NIMV over IMV. Propensity scores were included in a second logistic regression model used to assess the impact of NIMV on mortality in the study population. We tested the assumption that the logit was linear in quantitative variables by analyzing the estimated coefficients of designed variables representing the quartiles of the original variable distribution (30). When indicated, a second-order model or log-transformation of the variable was tested. If data could not be fitted with these approaches, the variable was divided into classes, and dummy variables were used.

Independent variables associated with mortality with a $p < .3$ were analyzed with a step-by-step, backward-forward approach in which different models were selected with a $p < .05$ criterion at the likelihood ratio test. In accordance with our hypothesis, the ventilatory approach and propensity score were both forced in the model. All tests were two-tailed, with a significance level of .05.

RESULTS

Of the 161,115 patients admitted to the 158 participating ICUs between 2002 and 2006, 1,302 (0.8%) met the inclusion criteria for this study (Fig. 1, Table 1). Over half (n = 725 of 1302; 56%) came from medical wards; the others were transferred from emergency departments (n = 328, 25%), surgical wards (n = 145, 11%), or other ICUs (n = 104, 8%). Upon admission to the ICU, 149 (11%) patients had neutropenia (defined as a white blood cell count below 500 cells/mm^3), 288 patients (22%) had ALI or ARDS, and 788 (61%) had failure of two or three organs. Analysis of cases with infection data (768 admitted in 2005–2006) revealed at least one infection at admission in 316 (41%).

As shown in Figure 1, only 274 (21%) of the patients were treated at admission with NIMV. In 68 (43%) of the units, none of the patients received NIMV, and these centers were therefore excluded from propensity score calculations. In the other ICUs, NIMV was prescribed with similar frequencies (mean 23.7% [SD: 14.2]; median 20.6% [first and third quartiles 10.5%–30.0%]).

Compared with patients receiving IMV from the outset, those initially treated with NIMV were generally younger, with lower SAPS II scores and higher Glasgow coma scale scores (Table 1). ALI was significantly more frequent in the NIMV group, but the prevalence of ARDS in the two groups was similar. The IMV and NIMV groups also had similar rates of organ failure after ICU admission (434 of 1028 [42%] vs. 120 of 274 [44%]; $p = .64$).

Analysis of patients with ALI or ARDS revealed no significant relation between mortality and type of ventilation (odds ratio [OR] 0.77, 95% CI 0.45–1.30; $p = .32$), although the IMV subgroup had significantly higher SAPS II scores (means:

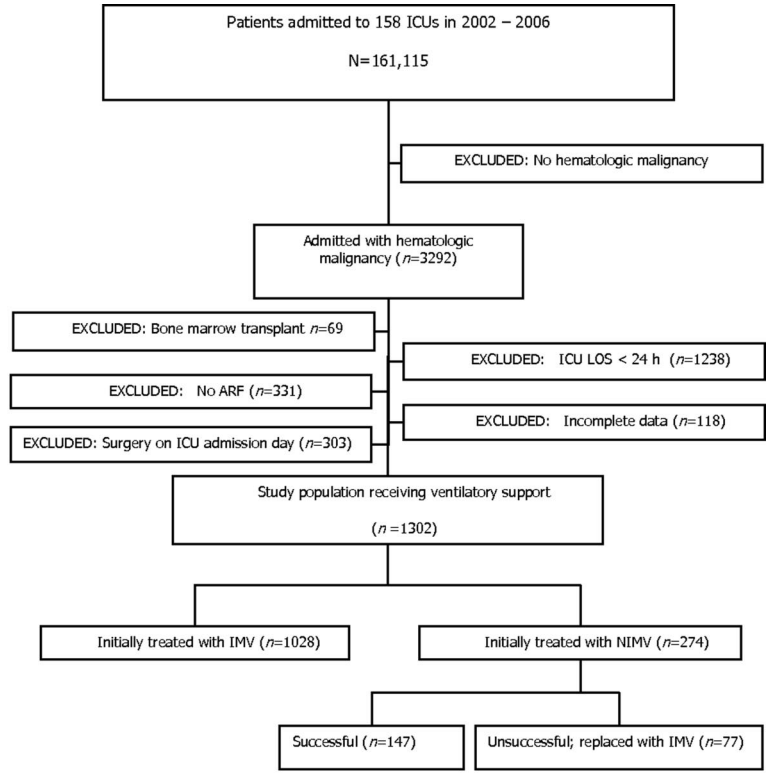

Figure 1. Study flow chart.

58 [19] vs. 49 [17] in the NIMV group, $p < .0001$). On the whole, however, the NIMV group exhibited significantly lower ICU and hospital mortality, shorter ventilation periods, and shorter ICU lengths of stay than the IMV group (Table 1). In multivariate analysis, after adjustments for group-assignment propensity scores, an initial NIMV trial was associated with lower hospital mortality than immediate recourse to IMV (OR 0.73, 95% CI 0.53–1.00; $p = .05$). Independent risk factors for mortality included ARDS, septic shock, stroke (on or after ICU admission), and higher SAPS II scores (Table 2) but not neutropenia (OR = 1.411; 95% CI 0.945–1.2106; $p = .0926$).

Over half (54%) of the NIMV patients never required endotracheal intubation (successful NIMV subgroup) (Fig. 1). In the other 127 (46%), NIMV was replaced with IMV after 3 ± 3 days (unsuccessful NIMV subgroup). These two subgroups were similar in terms of age, underlying diseases, organ failure rates at ICU admission, and reasons for ICU admission, but ALI/ARDS was almost twice as common in the unsuccessful NIMV subgroup (42% vs. 24%; $p = .002$) (Table 3). Multivariate analysis identified two major risk factors for NIMV failure: baseline illness severity reflected by SAPS II scores (OR = 2.012, 95% CI: 1.006–4.026; $p = .048$); and ALI/ARDS at admission (OR = 2.266, 95% CI: 1.346–3.816; $p = .002$). This model presented a p value of .0012 in the likelihood ratio test and a Hosmer-Lemeshow goodness of fit p of .76, and the two variables showed no colinearity.

In the NIMV subgroup with ALI/ARDS (n = 89), ICU and hospital mortality rates were higher in the 53 whose NIMV failed (OR 4.8, 95% CI 1.9–12.0; $p = .0007$ vs. the 36 with successful NIMV), although the two subgroups had similar mean SAPS II scores (50 ± 16 vs. 47 ± 17, respectively; $p = .51$).

Post-ICU-admission organ failure was significantly more common in the unsuccessful NIMV subgroup (80 of 127; 63% vs. 40 of 147; 27% in the successful NIMV subgroup, $p < .0001$). Most cases involved cardiovascular failure, which developed in 52 (41%) of the patients whose NIMV failed, and only 11 (7%) of those treated successfully with NIMV. As shown in Figure 2, postadmission septic shock was also more frequent in the unsuccessful NIMV subgroup (OR 3.06, 95% CI, 1.30–7.19, $p = .01$ vs. successful NIMV), but septic shock-related mortality rates were unrelated to NIMV outcome ($p = .47$).

Compared with patients intubated at ICU admission, those intubated after unsuccessful NIMV were significantly younger and had lower SAPS II scores. They were also more likely to come from medical wards (92 patients, 72% vs. 535, 52%; $p < .0001$), to be infected at ICU admission, and to develop organ failure during their ICU stay. Rates of septic shock and septic shock-related death were not significantly different in the IMV and total NIMV groups ($p = .10$ and $p = .27$, respectively) (Fig. 2), but septic shock was less common in the successful NIMV group than in patients treated with IMV (alone or after unsuccessful NIMV) ($p = .008$). Mortality in the successful NIMV group was also lower (66% vs. 80% and 77% for the IMV and unsuccessful NIMV groups, respectively) but not significantly so ($p = .12$). The subgroups with immediate and delayed IMV were also similar in terms of ICU length of stay and total duration of mechanical ventilation (Table 4).

Eight-nine of the 288 ALI/ARDS patients were treated with NIMV, but it was successful in only 36 (40%). Compared with the 199 ALI/ARDS patients who were intubated immediately, the 53 intubated after unsuccessful NIMV had significantly lower SAPS II scores (50 [16] vs. 58 [19], $p = .001$) and appreciably higher mortality, although this difference was not statistically significant (77% vs. 69%; $p = .23$, OR 1.55, 95% CI 0.76–3.14).

DISCUSSION

To our knowledge, this is the largest existing survey on real-life ICU ventilatory management of ARF in patients with hematologic malignancies. Our analysis of the 1302 cases described above indicates that: 1) ARF patients with hematologic malignancies represent <1% of total ICU admissions in Italy; 2) NIMV is attempted in only around 20% of these cases; 3) when successful, NIMV is generally associated with shorter mechanical ventilation periods and ICU stays, less severe postadmission infections, and lower ICU and hospital mortality; 4) after adjustment for the propensity to receive NIMV *ab initio*, the noninvasive approach is significantly associated with lower mortality than immediate IMV; and 5) roughly half the NIMV trials failed, and the patients had to be intubated. Al-

Table 1. Characteristics of the study population and the invasive mechanical ventilation and noninvasive mechanical ventilation subgroups

Population Characteristics	Total Population n = 1302	Invasive Mechanical Ventilation Group n = 1028	Noninvasive Mechanical Ventilation Group n = 274	*p*
Males–no. (%)	764 (59)	602 (59)	162 (59)	.95
Mean Age (SD), yrs	64 (15)	65 (15)	60 (16)	<.0001
Mean Simplified Acute Physiology Score II (SD)	56 (18)	58 (18)	49 (16)	<.0001
Median Glasgow Coma Score (interquartile range)	12 (8–15)	10 (7–15)	15 (14–15)	<.0001
Admission From Same Hospital–no. (%)	1053 (81)	807 (79)	246 (90)	<.0001
Clinical Conditions at Admission–no. (%)				
Neutropenia	149 (11.4)	103 (10.0)	46 (16.8)	.002
PaO_2/FIO_2				
≥200	459 (35.3)	384 (37.4)	75 (27.4)	<.0001
100–199	548 (42.1)	427 (41.5)	121 (44.2)	
<100	241 (18.5)	189 (18.4)	52 (20.0)	
Main Causes of Acute Respiratory Failure–no. (%)				
Atelectasis	49 (4)	41 (4)	8 (3)	.52
Infectious pneumonia	377 (29)	268 (26)	109 (40)	.0001
Inhalation pneumonia	25 (2)	24 (2)	1 (0.3)	.06
Pulmonary contusion	13 (1)	10 (1)	3 (1)	.07
Acute lung injury	167 (13)	110 (11)	57 (21)	<.0001
Adult respiratory distress syndrome	121 (9)	89 (9)	32 (12)	.13
Infections[a]–no. (%)				
Present on ICU admission	316 (41)	228 (39)	88 (50)	<.01
Onset during ICU stay	142 (18)	122 (21)	20 (11)	.01
Mean Duration of Care (SD), days				
Total hospital stay	30 (34)	30 (36)	30 (27)	.72
ICU stay	12 (15)	12 (16)	9 (10)	<.01
Duration of mechanical ventilation	—	11 (13)	4 (4)	<.0001
Mortality–no. (%)				
ICU				
All patients	617 (47)	511 (50)	106 (39)	<.01
Patients with acute lung injury or adult respiratory distress syndrome	171 of 288 (59)	119 of 199 (60)	52 of 89 (58)	.83
Hospital				
All patients	730 (56)	597 (58)	133 (49)	<.01
Patients with acute lung injury or adult respiratory distress syndrome	193 of 288 (67)	137 of 199 (69)	56 of 89 (63)	.32

ICU, intensive care unit.

[a]Information on infections is available only for 768 patients admitted during 2005–2006 (591 invasive mechanical ventilation group, 177 noninvasive mechanical ventilation group). None of the patients who had shock or stroke on admission received noninvasive mechanical ventilation group.

Table 2. Risk factors for mortality

Factor	Odds Ratio[a] Point Estimate (95% Confidence Limits)
Initial ventilatory support: Noninvasive Mechanical Ventilation vs. Invasive Mechanical Ventilation	0.73 (0.53–1.00)
Hematologic Malignancy: Admission Diagnosis vs. Comorbidity	1.34 (1.03–1.73)
Admission from Another Intensive Care Unit vs. Medical Ward	0.98 (0.60–1.60)
Admission from Emergency Department vs. Medical Ward	0.66 (0.49–0.88)
Admission from Surgical Ward vs. Medical Ward	0.62 (0.42–0.92)
Acute Lung Injury	1.69 (1.16–2.47)
Adult Respiratory Distress Syndrome	2.09 (1.32–3.31)
Stroke	2.29 (1.11–4.75)
Septic Shock	2.43 (1.61–3.65)
Other Type of Shock	2.16 (1.24–3.76)
Coagulopathy	1.59 (1.13–2.23)
Coma	1.68 (1.05–2.69)
Age	1.01 (1.01–1.02)
Simplified Acute Physiology Score II (each 4-point increase)	4.66 (2.98–7.28)
Propensity score	5.07 (1.40–18.32)

[a]Number of observations: 1302; Likelihood Ratio: chi-square: 195.39; Degrees of freedom: 15; $p < .0001$; association of predicted probabilities and observed responses: Percent concordant: 73.1; Percent discordant: 26.7; Somers' D: 0.46; c statistic: 0.73.

Stroke, any form of shock, and coma refers to condition occurring after the study inclusion.

though hospital mortality was similar in these patients and those intubated at admission, unsuccessful NIMV in patients with ALI/ARDS was associated with 70% mortality.

ARDS, septic shock, and higher SAPS II scores were all independent risk factors for mortality. ARF is a leading cause of ICU admission among patients with hematologic malignancies or solid tumors (31), and the prognosis has always been regarded as poor. Over the past decade, however, higher survival rates have emerged from several observational studies (31–33), and the improvement has been at least partly attributed to the early use of NIMV (33–35). In a randomized trial, noninvasive face-mask-mediated pressure-support ventilation of immunosuppressed patients with ARF was associated with significantly better gas exchange, lower intubation rates, and fewer complications, as compared with supplemental oxygen alone (36). The benefits

Table 3. Comparison of the successful and unsuccessful noninvasive mechanical ventilation groups

Group Characteristics	Successful NIMV (n = 147 [54%])	Unsuccessful NIMV (n = 127 [46%])	*p*
Males–no. (%)	83 (56)	79 (63)	.30
Mean Age (SD), yrs	60 (17)	60 (14)	.73
Mean Simplified Acute Physiology Score II (SD)	47 (17)	51 (15)	.07
Median Glasgow Coma Scale (interquartile range)	15 (14–15)	15 (14–15)	.95
ALI-ARDS at Admission–no. (%)			
ALI	21 (14)	36 (28)	<.01
ARDS	15 (10)	17 (13)	.41
Infections[a]–no. (%)			
Present at ICU admission	46 (31)	42 (33)	.60
Onset during ICU stay	1 (1)	19 (15)	<.0001
Organ Failure–no. (%)			
Present at ICU admission	141 (96)	121 (95)	.80
Onset during ICU stay	40 (27)	80 (63)	.00005
Mean Duration of Care (SD)–days			
Total hospital stay	29 ± 24	32 ± 30	.39
ICU stay	6 ± 5	14 ± 12	<.0001
Duration of NIMV	5 ± 4	3 ± 3	<.0001
Mortality–no. (%)			
ICU mortality			
All patients	28 (19)	78 (61)	<.0001
Patients with ALI or ARDS	13 of 36 (36)	39 of 53 (74)	.0005
Hospital mortality			
All patients	50 (34)	83 (65)	<.0001
Patients with ALI or ARDS	15 of 36 (42)	41 of 53 (77)	.001

ALI, acute lung injury; ARDS, adult respiratory distress syndrome; ICU, intensive care unit; NIMV, noninvasive mechanical ventilation.

[a]Information on infections was available only for 768 patients admitted during 2005–2006 (591 invasive mechanical ventilation group, 177 NIMV group).

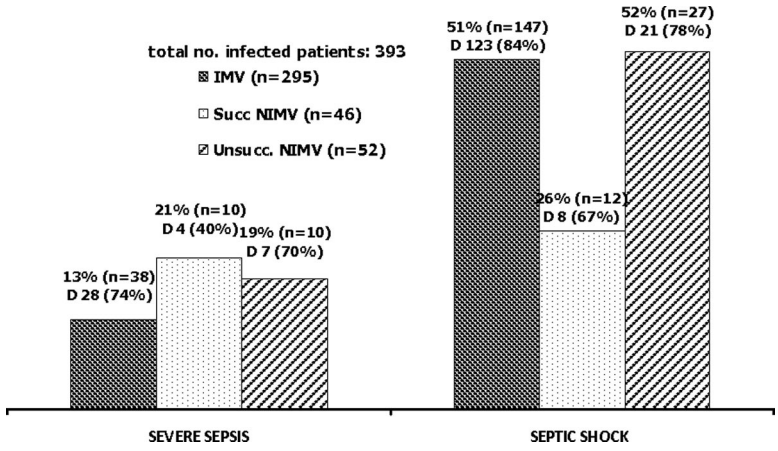

Figure 2. Severe sepsis and septic shock occurring after intensive care unit admission. Data are available only for patients admitted in 2005 or 2006. *Bars* represent sepsis or septic shock rates expressed as percentages of infected patients in each group. *IMV*, invasive mechanical ventilation; *NIMV*, noninvasive mechanical ventilation; *D*, number (percentage) of infections ending in death.

were particularly remarkable in patients with hematologic malignancies, prompting the authors to propose NIMV as the method of choice for ventilatory support in these patients (36). Later, however, a "real-world" survey conducted in a teaching hospital in France found that NIMV failure requiring intubation and conventional mechanical ventilation occurs frequently in this population (54%), particularly when NIMV is started late, and is associated with hospital mortality of 79% (34).

We analyzed over 1,300 patients with hematologic malignancies admitted to Italian ICUs for ARF between 2002 and 2006, and their overall survival rate (53%) is consistent with recent figures reported for myeloma patients admitted to ICUs (13). Our main objectives, however, were to discover how this outcome is affected by the initial approach to ventilatory support, to identify risk factors for NIMV failure, and to determine how NIMV failure influences case outcomes.

General guidelines for prescribing NIMV were identical in all participating centers (26), but there was a certain degree of inter-unit variability because actual decisions depended on the attending ICU physician's clinical judgment. Consequently, differences in mortality might reflect the effects of the chosen approach, the effects of clinical features that determined the choice, or both. The risk of an allocation bias was minimized by adjustment for individual patient scores representing their propensity to be ventilated noninvasively at ICU admission. Inclusion of this score in a multivariate model allowed us to estimate the impact of NIMV on mortality under conditions in which each patient is equally likely to receive this type of ventilatory support, that is, conditions resembling those of a randomized trial. It cannot eliminate differences in the distribution of unmeasured confounders, but it provides the best estimate of treatment efficacy that can be obtained with observational data.

This analysis revealed that, on the whole, an initial NIMV trial significantly reduced mortality by 27%. As noted by others (35–38), NIMV failure is common in this patient population (around 50% in our study). Major independent risk factors for this outcome were illness severity reflected by the SAPS II score and the presence at admission of ALI/ARDS, and these findings are also consistent with the conclusions of surveys conducted in nonselected ARF patients (36). It is also true that ICU mortality in our unsuccessful NIMV subgroup clearly exceeded that of the group intubated at admission (61% vs. 50%, $p < .01$), but this effect was compensated for by lower mortality when NIMV was successful (19%, Table 2), so that the net effect of attempting NIMV was positive.

NIMV is unsuitable for some patients with hematologic malignancies. Severe respiratory failure (e.g., that associated with ALI or ARDS) may be an indication for early intubation. These conditions are invariably associated with high mortality, regardless of the type of ventilatory support provided. In another recent real-life study, IMV of immunocompetent patients with ALI or ARDS and a mean SAPS II score of 36 was associated with a mortal-

Table 4. Comparison of invasive mechanical ventilation and unsuccessful noninvasive mechanical ventilation groups

Group Characteristics	Invasive Mechanical Ventilation (n = 1028 [79%])	Unsuccessful Noninvasive Mechanical Ventilation (n = 127 [46%])	*p*
Males–no. (%)	602 (59)	79 (63)	.44
Mean Age (SD), yrs	64 (15)	60 (14)	<.01
Mean Simplified Acute Physiology Score II (SD)	58 (18)	51 (15)	<.0001
Median Glasgow Coma Score (interquartile range)	10 (7–15)	15 (14–15)	<.0001
Organ Failure at Admission	1002 (97)	121 (95)	.16
ALI–ARDS at Admission–no. (%)			
ALI	110 (11)	36 (28)	<.0001
ARDS	89 (9)	17 (13)	.08
Infections–no. (%)[a]			
Present at ICU admission	228 (39)	42 (52)	.02
Onset during ICU stay	122 (21)	19 (23)	.56
Organ Failure–no. (%)			
Present at ICU admission	1002 (97)	121 (95)	.16
Onset during ICU stay	434 (42)	80 (63)	<.0001
Mean Duration of Care (SD)–days			
Total hospital stay	29 (36)	32 (30)	.44
ICU stay	12 (16)	14 (12)	.27
Duration of mechanical ventilation	11 (13)	10 (11)	.63
Mortality–no. (%)			
ICU mortality			
All patients	511 (50)	78 (61)	.01
Patients with ALI or ARDS	119 of 199 (60)	39 of 53 (74)	.07
Hospital mortality			
All patients	597 (58)	83 (65)	.12
Patients with ALI or ARDS	137 of 199 (69)	41 of 53 (77)	.23
Mortality after ICU stay	88 (17)	5 (10)	.22

ALI, acute lung injury; ARDS, adult respiratory distress syndrome; ICU, intensive care unit.

[a]Information on infections was available only for 768 patients admitted during 2005–2006 (591 invasive mechanical ventilation group, 177 noninvasive mechanical ventilation group).

ity rate of 56% (28). Failure of first-line NIMV was associated with similar rates (53%) in a study of 147 patients with ARDS (mean SAPS II of 38) (38). The ALI/ARDS patients we studied were much sicker than these, with compromised immunity and a mean SAPS II score of 50, and in this subgroup NIMV failure was associated with 77% mortality. The rate was appreciably but not significantly lower in those intubated at admission (69%). Therefore, it is difficult to say whether this outcome is more strongly related to the pretreatment severity of their illness or the delay in their intubation.

A minor shortcoming of our study is the absence of population stratification according to the type of hematologic malignancy. The admission diagnoses entered on the electronic form were not detailed enough for this level of distinction. Previous reports, however, indicate that—unlike bone marrow transplantation (an exclusion criterion in our study)—the underlying hematologic malignancy is not prognostically significant in this setting (34, 39). A more important shortcoming is the study design, which did not allow definitive conclusions regarding the best first-line approach to ARF in this population. In observational studies, investigators have no control over the probability that a patient will be assigned to one treatment or another. By equalizing the patients' probability of receiving IMV or NIMV, propensity score regression adjustment optimized our chances of obtaining an accurate estimate of treatment efficacy from observational data.

CONCLUSIONS

With the limitations discussed above, our findings support the first-line use of NIMV for management of ARF in patients with hematologic malignancies. They also emphasize the importance of preventing NIMV failure in these patients, which is associated with high mortality. This goal obviously requires adequate equipment and optimal staff training, but careful patient selection and effective protocols for early detection of NIMV failure also play important roles, reducing the risk and complications of emergency intubation. Further study may be needed to explore the possible benefits and/or risks of NIMV in patients with ALI or ARDS.

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APPENDIX

List of Study Participants

Acciarri Claudia (Ascoli Piceno), Achilli Dorella (Ascoli Piceno), Alberti Arnaldo (Porto Viro - RO), Alborghetti Armando (Ponte San Pietro - BG), Archi Davide (Lodi), Badii Flavio (San Donà di Piave - VE), Barattini Massimo (Florence), Barbagli Remo (Florence), Bartoccini Arcangelo (Borgomanero - NO), Bassi Francesco (Cinisello Balsamo - MI), Beck Eduardo (Desio - MI), Bellorini Mario (Tradate - VA), Benanti Cesare (Pescia - PT), Benelli Piergiovanni (Lodi), Berardino Maurizio (Turin), Bernasconi Mara Olga (Rovigo), Bertolini Roberta (Pisa), Bianchina Andrea (Montebelluna - TV), Biolino Piera (Turin), Blasetti Angelo (Avezzano - AQ), Bogatto Riccardo (Ivrea - TO), Bolfiglio Monica (Lavagna - GE), Bolizzoli Manuela (Florence), Bonaccorso Giuseppina (Padua), Bonanno Roberto (Lacco Ameno - NA), Bonfà Andrea (Prato - PO), Bonifetto Giorgio (Feltre - BL), Borreggine Donati (San Donà di Piave - VE), Bosco Donatella (Pescara), Bottari Walter (Reggio Emilia), Bottinelli Maristella (Lecco), Breschi Cesare (Pesaro - PU), Bressan Silvia (Turin), Brunoli Emanuela (Macerata), Buzzetti Virginio (Orbetello Scalo - GR), Calicchio Giuseppe (Salerno), Calva Sally (Turin), Carinci Pierpaolo (Lanciano - CH), Carnevale Livio (Pavia), Casadei Edith (Siena), Casagrande Lucia (Treviso), Casalini Pierpaolo (Faenza - RA), Casciani Massimo (Rome), Casciani Massimo - Molino Fausto Maria (Rome), Castiglione Giacomo (Catania), Cavallo Renata (Turin), Chieregato Arturo (Cesena - FC), Chinelli Elena (Bologna), Chini Giuseppe (Borgo San Lorenzo - FI), Ciritto Nunzio

(Cefalù - PA), Coaloa Maddalena (Savigliano - CN), Coita Paolo (Savigliano - CN), Colombo Riccardo (Milan), Corsini Walter (Carrara - MS), Costanzo Eleonora (Asti), Cottignoli Tito (Lugo di Romagna - RA), Crema Luciano (Cremona), Crestan Ezio (Lecco), Croce Giovanna (Padua), Dal Cero Paolo - Possamai Clemente (Conegliano - TV), Daniela Boccalatte (Lucca), De Blasio Elvio (Benevento), De Negri Pasquale (Rionero in Vulture - PZ), DE Sarto Paolo (Massa), Di Masi Pierfrancesco (Castellana Grotte - BA), Di Melis Piergiorgio (Lucca), Di Pasquale Dino (Pontedera - PI), Donatiello Giuseppe (Milan), Enrico Arditi (Genova), Fabbri Emilio (Forlì - FC), Fabbri Lea Paola (Florence), Fabbri Piergiorgio (Palermo), Fabi Maria Cristina (Fano - PU), Favero Alessandra (Milan), Favetta Paola (Perugia), Febbrari Paolo (Brescia), Federica Rottoli (Bergamo), Federici Cinzia (Rossano - CS), Ferla Francesco (Cefalù - PA), Ferrari Baliviera Elisabetta (Rome), Festa Maurilio (Turin), Fiore Gilberto (Moncalieri - TO), Galeotti Elsa (Feltre - BL), Gamberini Emiliano (Cesena - FC), Garelli Alberto (Ravenna), Garofalo Giuseppe (Catania), Garzilli Tiziana (Perugia), Gavioso Marina (Asti), Giacopuzzi Luigi (Negrar - VR), Gianni Massimo (Aosta), Giannoni Stefano (Empoli - FI), Giorgio Paganini (Sanremo - IM), Giudici Daniela (Milan), Giugiaro Pier Mario (Ciriè - TO), Gorietti Adonella (Perugia), Grassi Paolo (Figline Valdarno - FI), Greco Maurizio (Ariano Irpino - AV), Guadagnucci Alberto (Massa), Holzer Gianni (Lecco), Isetta Michele (Genova), Lapolla Antonio (Genova), Lavacchi Luca (Pistoia), Lazzaro Francesco (Fermo - AP), Livigni Sergio (Turin), Lorenzo Odetto (Orbassano - TO), Luisa Ranzini (Milan), Madonna Roberto (Grosseto), Magatti Maria Federica (Como), Maggiolo Carlo (Adria - RO), Maitan Stefano (Faenza - RA), Malacarne Paolo (Pisa), Malinconi Alba (Este - PD), Mangani Valerio (Florence), Mantovani Giorgio (Ferrara), Marafon Silvio (Vicenza), Marchesi Gianmariano (Bergamo), Marco Chiarello (Camerino - MC), Maria Grazia Visconti (Cernusco sul Naviglio - MI), Mario Tavola (Lecco), Marson Franco (Treviso), Mastroianni Alessandro (Chieri - TO), Mastropierro Rosa (Brescia), Mazzacane Pasquale (Benevento), Meloni Alessandra (Sassari), Messina Mariana (Olbia - OT), Meucci Monica (Aosta), Miglioranzi Renzo (Pieve di Coriano - MN), Molino Fausto Maria (Rome), Montani Cinzia (Milan), Moria Bernard (Belluno), Morigi Aristide (Bologna), Murri Viscardo (Lanciano - CH), Murru Salvatore (Cagliari), Nardi Giuseppe (Rome), Nardin Massimiliano (Pistoia), Nascimben Ennio (Treviso), Natalini Giuseppe (Brescia), Negri Giovanni (Magenta - MI), Negro Giancarlo (Casarano - LE), Neri Massimo (Bologna), Nicola Rossi (Monza - MI), Nicolini Andrea (Lido di Camaiore - LU), Nuovo Domenico (Turin), Oliviri Carlo (Novara), Oronzo Martino (Matera), Pacini Daniela Maria (Genova), Palmer Maurizio (Aversa - CE), Panella Luigi (L'Aquila), Papiri Silvano (San Benedetto del Tronto - AP), Parma Alberto (Milan), Pasqualino Quattrocchi (Catania), Pastorelli Mauro (Pinerolo - TO), Pastorini Simonetta (Camposampiero - PD), Pedullà Armando (Antella - FI), Pegoraro Maurizio (Castelfranco Veneto - TV), Pelagatti Cecilia (Florence), Pessina Carla (Rho - MI), Pezza Brunello (Benevento), Pezzi Angelo (Milan), Piccioni Giuseppe (Manerbio - BS), Pincirolo Donatella (Legnano - MI), Piredda Giuseppe (Sassari), Pizzaballa Marialuisa (Zingonia - BG), Poggetto Luigi (Pescia - PT), Poole Daniele (Belluno), Potalivo Antonella (Bologna), Pugnetti Enrica (Milan), Pulici Marco (Milan), Racca Fabrizio (Moncalieri - TO), Radaelli Gianluigi (Monza - MI), Ricci Alessandro (Bologna), Riedo Roberto (Desio - MI), Righini Erminio (Lagosanto - FE), Romitti Mario (Piacenza), Rossi Giancarlo (Livorno), Rossi Maurizio (Menaggio - CO), Rossi Simona (Rho - MI), Rotelli Stefano (Milan), Salcuni Maria Rosa - Bolloni Umberto (Ivrea - TO), Segala Vincenzo (Turin), Servadio Giorgio (Busto Arsizio - VA), Sicignano Alberto (Milan), Spadini Elisabetta (Parma), Staccioli Paola (Pistoia), Tartari Stefano (Trecenta - RO), Teresa Bartoli (Antella - FI), Tetamo Romano (Palermo), Tinacci Silvia (Fucecchio - FI), Todesco Livio (Cittadella - PD), Tommasoni Gabriele (Manerbio - BS), Torresi Sandro (Camerino - MC), Torta Mauro (Turin), Tripepi Carlo (Monselice - PD), Ughi Ludovica (Milan), Vaj Monica (Turin), Vecchiarelli Pietro (Viterbo), Vendrame Giordano (Cantù - CO), Vespignani Maria Giovanna (Imola - BO), Viozzi Alberto (Fermo - AP), Vivaldi Nicoletta (Alessandria), Zamponi Edoardo (Novara), Zanello Marco (Bologna), Zappa Sergio (Brescia), Zocaro Rosamaria (Pescara), Zuccaro Francesco (Matera).