Influence of the Admission Pattern on the Outcome of Patients Admitted to a Respiratory Intensive Care Unit: Does a Step-Down Admission Differ From a Step-Up One?

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BACKGROUND: The outcomes of patients admitted to a respiratory ICU (RICU) have been evaluated in the past, but no study has considered the influence of location prior to RICU admission. METHODS: We analyzed prospectively collected data from 326 consecutive patients admitted to a 7-bed RICU. The primary end points were survival and severity of morbidity-related complications, evaluated according to the patient's location prior to RICU admission. Three admission pathways were considered: step-down for patients transferred from the ICUs of our hospital; step-up for patients coming from our respiratory wards or other medical wards; and directly for patients coming from the emergency department. The secondary end point was the potential influence of several risk factors for morbidity and mortality. RESULTS: Of the 326 subjects, 92 (28%) died. Overall, subjects admitted in a step-up process had a significantly higher mortality ($P < .001$) than subjects in the other groups. The mortality rate was 64% for subjects admitted from respiratory ward, 43% for those from medical wards, and 18% for subjects from both ICU and emergency department (respiratory ward vs medical ward $P = .04$, respiratory ward vs emergency department $P < .001$, respiratory ward vs ICU $P < .001$, medical ward vs emergency department $P < .001$, and medical ward vs ICU $P < .001$). Subjects admitted from a respiratory ward had a lower albumin level, and Simplified Acute Physiology Score II was significantly higher in subjects following a step-up admission. About 30% of the subjects admitted from a respiratory ward received noninvasive ventilation as a "ceiling treatment." The highest odds ratios related to survival were subject location prior to RICU admission and female sex. Lack of use of noninvasive ventilation, younger age, female sex, higher albumin level, lower Simplified Acute Physiology Score II, higher Barthel score, and absence of chronic heart failure were also statistically associated with a lower risk of death. CONCLUSIONS: The pathway of admission to a RICU is a determinant of outcome. Patients following a step-up pattern are more likely to die. Other major determinants of survival are age, nutritional status and female sex. *Key words: respiratory ICU; critically ill patient; noninvasive ventilation; weaning; ICU; acute respiratory failure.* [Respir Care 2013;58(12):2053–2060. © 2013 Daedalus Enterprises]

Introduction

Respiratory ICUs (RICUs) have developed around the world as specialized single organ units providing an intermediate level of care between that supplied in ICUs and in general wards.[1] This model of care has been generally

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considered as an example of good management of hospital resources, enabling effective control of costs,[2] although its actual cost-effectiveness has been questioned.[3] According to the European Respiratory Society, a RICU is defined by the following characteristics: a nurse-patient ratio > 1:3, the presence of multifunctional monitors and life support ventilators, and the possibility of applying both invasive ventilation and noninvasive ventilation (NIV) in patients with lung failure or more than one organ failure.[1] Depending on the patient's previous level of care, a RICU can provide: step-up care when admitting a patient transferred from a general ward, needing specific treatments, such as NIV or invasive ventilation and/or close monitoring, for an acute respiratory failure episode that developed during the hospital admission; or step-down care when a patient no longer requires all the facilities of an ICU but is not ready to be transferred to a general medical ward because of specific care needs (eg, management of tracheotomy) or still requires invasive ventilation. The third pathway of admission is from the emergency department. It is intuitive that patients who are getting better (ie, transferred from an ICU) may have more favorable outcomes than those who are getting worse (ie, those transferred from a medical ward), but this point has never been systematically investigated in the specific environment of the RICU, in which admissions occur from both directions (up and down), as opposed to an ICU, in which the admission flow is always from below (ie, only patients getting worse are admitted). Previous studies have addressed this issue in the ICU. For example, Gerber et al found that transfer of patients to a tertiary care ICU from the emergency department of a referring hospital was associated with significantly better outcomes than transfer from a referring hospital ICU,[4] confirming the observations of other authors.[5,6] It is unknown whether or not the patient's location prior to RICU admission influences in-hospital survival. An analysis of data on this issue could help clinicians and hospital administrators to better understand the role and effectiveness of the RICU. Surprisingly, none of the studies assessing patient characteristics and outcomes have considered these 3 admission patterns as variables potentially influencing outcomes. We therefore analyzed survival, patients' clinical characteristics at admission, and the variables that best correlated with patient outcome, in an RICU in a large academic hospital. We also analyzed the data with exclusion of patients who had do-not-intubate (DNI) orders.

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QUICK LOOK

Current knowledge

Respiratory ICUs and intermediate care units care for patients who require mechanical ventilation but no longer require intensive care. These units improve weaning success and reduce costs.

What this paper contributes to our knowledge

The pathway of admission to a respiratory ICU is a major determinant of outcome. Patients transferred, because of clinical deterioration, from a medical or respiratory ward (step-up pattern) are more severely ill and have worse mortality than those transferred from an ICU (step-down pattern). Age, female sex, and nutritional status were major determinants of survival.

Methods

In an analysis of data prospectively collected and entered into a database, we evaluated 326 consecutive patients admitted over a 22-month period into our 7-bed RICU, with 3 beds located in a single room.

The study protocol was approved by the ethical and scientific committee of Azienda Opedaliera Universitaria Sant Orsola-Malpighi, Bologna, Italy. Subjects gave written consent to participation in the study: however, 34 subjects were not able to sign the consent form, and in these cases a relative signed on their behalf. In 18 of these cases the subject was later able to sign the consent form.

The primary end point of the study was the impact of the subject's location prior to RICU admission on survival and severity score. The 3 different pathways of admission were classified as follows:

- Step-down: admitted from one of the 3 ICUs in our hospital (general ICU, post-surgical ICU, and post-transplant/extracorporeal membrane oxygenation [ECMO] ICU)
- Step-up: admitted from a ward in our hospital (respiratory, internal medicine, gerontology, cardiology, physical therapy, orthopedic, or hematology)
- Directly: admitted from the emergency department

We recorded age, sex, admission comorbidities, admission albumin level, worst Simplified Acute Physiology Score II (SAPS II) measured within the first 24 hours of RICU admission,[7] Barthel index, blood-gas values, long-term-oxygen or mechanical ventilation before hospitalization, invasive ventilation or NIV in the RICU, hospital stay before RICU admission, causes of acute respiratory failure (eg, exacerbation of COPD, heart failure, pneumonia, or ARDS),[8] destination after discharge, and new prescription of invasive ventilation, NIV, or oxygen therapy at discharge. Subjects were considered to have previously diagnosed COPD if post-bronchodilator FEV_1/FVC was ≤ 0.7.[9] The diagnosis of hypoxemic respiratory failure was based on a $P_{aO_2}/F_{IO_2} \leq 300$ mm Hg.[10] The secondary end point was the potential influence of the above-mentioned variables, except the destination at discharge and the new prescription of oxygen and/or ventilation, on survival, both according to the location prior to RICU admission and as a whole group.

Statistical Analysis

With regards to the 3 different patterns of admission to the RICU, for the data analysis we considered our respiratory ward as a stand-alone unit inside the step-up pathway, due to the fact that the RICU is located inside the respiratory ward and shares the same medical staff.

Results are expressed as mean ± SD for continuous variables, and percentages for categorical variables. Demographic and disease characteristics were compared among the 4 provenances (respiratory ward, medical ward, emergency department, and ICU), using the Pearson chi-square test for categorical variables and one-way analysis of variance, followed by the Scheffé post hoc test for continuous variables.

We used univariate and multivariate logistic regression analyses to investigate mortality-related risk factors and to determine independent risk factors related to mortality. The following variables were entered into the univariate and multivariate analyses: age, sex, number of comorbidities, albumin level, worst SAPS II within the first 24 hours of RICU admission, Barthel Index, blood-gas values, long-term oxygen or ventilatory therapy before hospitalization, invasive ventilation or NIV on RICU admission, hospital stay before RICU admission, and causes of acute respiratory failure. The odds ratios were used to identify factors associated with survival. A P value $< .05$ was considered statistically significant. Statistical analyses were conducted with statistics software (Stata/IC, StataCorp, College Station, Texas).

Results

Primary Outcomes

The Figure illustrates the flow of subjects admitted to our RICU during the study period, and their mortality rates. Ninety-two subjects (28%) died. Overall, the step-up subjects (from a respiratory ward or medical ward) had significantly higher mortality ($P < .001$) than the step-down subjects (from an ICU) or the subjects from the emergency department. The statistical differences in mortality between the units were: $P = .04$ for respiratory ward versus medical ward, $P < .001$ for respiratory ward versus emergency department, $P < .001$ for respiratory ward versus ICU, $P < .001$ for medical ward versus emergency department, and $P < .001$ for medical ward versus ICU.

Sixty subjects were from the post-surgical ICU, 45 from the general ICU, and 3 from the post-transplant/ECMO ICU. There was no statistically significant difference in mortality rate between subjects from the post-surgical ICU (11/60, 18%) and the general ICU (7/45, 16%). The causes of death were mainly related to sepsis or end-stage pulmonary disease, in particular in subjects with a DNI order. Overall, of the 326 subjects, 27 with a DNI order died, accounting for 29% of the 92 subjects who died in the study. These 27 subjects comprised 8 with advanced cancer (8% of all deaths), 10 with end-stage pulmonary fibrosis (11% of all deaths), and 9 with end-stage COPD (10% of all deaths), who had refused invasive treatments (Table 1).

The mortality rate in the 285 subjects without DNI order was similar to the overall mortality rate, with the same statistical difference between step-up and step-down admission ($P < .001$). Of these 285 subjects, 51 (18%) died:

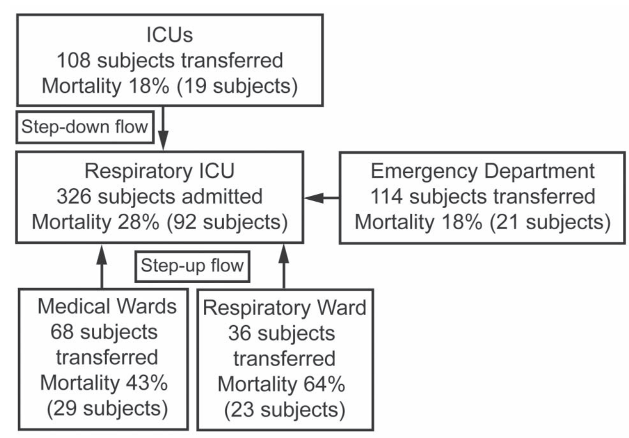

Figure. Admission to the respiratory ICU from other departments.

Table 1. Causes of Death

	Subjects no. (%)
Severe sepsis or septic shock	33 (36)
Refractory respiratory acidosis	9 (10)
ARDS	2 (2)
Ischemic heart attack	21 (23)
Do-not-intubate order	27 (29)
End-stage idiopathic pulmonary fibrosis	10 (11)
End-stage cancer	8 (8)
End-stage COPD	9 (10)

Table 2. Subject Characteristics on Admission to the Respiratory ICU, Based on the Subject's Previous Location

	Subject's Previous Location				P Between Groups	P After Scheffé Post Hoc Test
	Respiratory Ward	Medical Ward	Emergency Department	ICU		
Age, y	77.36 ± 9.24	70.46 ± 17.55	72.28 ± 16.25	69.16 ± 15.87	.050	.009 for respiratory ward vs ICU .21 for respiratory ward vs medical ward .42 for respiratory ward vs emergency department .90 for medical ward vs emergency department .96 for medical ward vs ICU .54 for emergency department vs ICU
Male/female, no.	25/11	32/36	52/62	53/55	.09	
Simplified Acute Physiology Score II	43.47 ± 11.45	38.34 ± 15.91	34.38 ± 12	32.83 ± 12.65	< .001	.30 for respiratory ward vs medical ward .005 for respiratory ward vs emergency department .001 for respiratory ward vs ICU .27 for medical ward vs emergency department .050 for medical ward vs ICU .85 for emergency department vs ICU
Albumin, g/dL	2.93 ± 0.50	3.22 ± 0.49	3.46 ± 0.52	3.23 ± 0.52	< .001	.06 for respiratory ward vs medical ward .001 for respiratory ward vs emergency department .03 for respiratory ward vs ICU .03 for medical ward vs emergency department > .99 for medical ward vs ICU .01 for emergency department vs ICU
Time prior to admission, d	16.3 ± 18.6	14.8 ± 19.81	2.32 ± 4.10	14.9 ± 18.16	< .001	.97 for respiratory ward vs medical ward < .001 for respiratory ward vs emergency department .97 for respiratory ward vs ICUs < .001 for medical ward vs emergency department > .99 for medical ward vs ICU < .001 for emergency department vs ICU
Age-adjusted Charlson Comorbidity Index	8.69 ± 2.31	6.49 ± 1.89	4.67 ± 2.35	5.51 ± 2.19	.001	< .01 for respiratory ward vs emergency department < .02 for respiratory ward vs ICU .06 for respiratory ward vs medical ward .07 for medical ward vs emergency department .34 for medical ward vs ICU .27 for emergency department vs ICU
Causes of exacerbation, %						
COPD exacerbation	64	61	73	54	.04	
Hypoxic respiratory failure	33	52	35	49	.03	
Chronic heart failure	58	52	53	49	.80	

± Values are mean ± SD.

12/25 (48%) from the respiratory ward, 21/60 (35%) from a medical ward, 8/101 (8%) from the emergency department, and 10/99 (10%) from an ICU.

The subjects' characteristics at admission to the RICU, based on their previous location, are presented in Table 2. Subjects admitted from the respiratory ward had a significantly lower serum albumin level than those from an ICU or the emergency department ($P = .03$ and $P = .001$, respectively). SAPS II was significantly higher in the step-up subjects (from a medical or respiratory ward) than in the step-down subjects ($P = .005$ for respiratory ward vs emergency department, $P = .001$ for respiratory ward vs ICU, and $P = .050$ for medical ward vs ICU), except for medical ward versus emergency department. Almost all the subjects had more than one comorbidity, as shown by the Charlson Comorbidity Index scores,[11] which were significantly higher in subjects who came from the respiratory ward ($P < .01$ for respiratory ward vs emergency department, $P < .02$ for respiratory ward vs ICU). The causes of admission were sometimes multiple, with overlap between groups (eg, COPD exacerbation plus pneumonia or heart failure) and rather homogenously distributed, but with little difference according to the location prior to RICU admission. The time prior to RICU admis-

Table 3. Ventilation Mode on Admission and at Discharge

	Subjects, no. (%)			
	Respiratory Ward	Medical Ward	Emergency Department	ICU
At RICU admission				
Noninvasive ventilation	9 (9)	20 (20)	52 (51)	20 (20)
Noninvasive ventilation as ceiling treatment (in do-not-intubate subjects)	11 (27)	8 (19)	13 (32)	9 (22)
No ventilation	12 (14)	20 (24)	28 (34)	23 (28)
Invasive ventilation	4 (11)	20 (20)	21 (19)	56 (50)
At RICU discharge				
Noninvasive ventilation	16 (21)	18 (23)	29 (38)	14 (18)
Invasive ventilation	2 (4)	18 (35)	8 (15)	24 (46) 20 tracheotomies
No ventilation	18 (9)	33 (17)	76 (39)	70 (35)

RICU = respiratory ICU

sion was statistically different between the groups, particularly between the subjects from the emergency department and those from the other locations.

As shown in Table 3, overall about 25% of the subjects did not require any form of ventilation. More than 50% of the subjects transferred from an ICU were invasively ventilated (either via an endotracheal tube or tracheotomy). About 30% of the subjects transferred from our respiratory ward received NIV as a "ceiling treatment." At discharge the majority of subjects did not need any ventilatory support. No statistical differences were found between the 4 groups in terms of ventilation method on admission. Less than 6% of the subjects were discharged home directly from the RICU; most of the subjects (62%) were transferred from the RICU to our respiratory ward. Only 3% of the survivors needed re-admission to an ICU.

Secondary Outcomes

As shown in Table 4, the univariate analysis shows that the factor with the highest odds ratio related to survival was location prior to RICU admission. Subjects transferred from the emergency department or ICU had the highest chance of survival. Lack of NIV use, younger age, female sex, higher albumin level, lower SAPS II, higher Barthel score, longer hospital stay prior to RICU admission, and absence of chronic heart failure were statistically associated with a lower risk of death.

The multivariate analysis found that some of those variables lost their individual power. Considering categorical variables, the probability of survival was almost 6 times higher for women, whereas subjects admitted from the respiratory ward had about a 4 times lower probability of survival than those admitted from the emergency department. Considering the continuous variables, survival probability decreased by 8% for every one point increment of SAPS II. In contrast, for every 1 g increase of albumin concentration, the survival probability was 3 times higher.

Table 4. Prognostic Indices for Survival

	Odds Ratio	*P*
Univariate logistic regression		
Age (per 1 year increase)	0.96	.001
Female sex	2.62	.001
Location before RICU admission	7.32	.001
Noninvasive ventilation vs no ventilation at admission	0.51	.041
Albumin (per 1 g/dL increase)	3.80	.01
Simplified Acute Physiology Score II (per 1 unit increase)	0.92	.001
Heart failure	0.53	.001
Barthel index (per 1 unit increase)	1.04	.001
Days before RICU admission (per 1 day)	0.98	.011
Multivariate analysis		
Sex (F vs M)	5.76	.001
Location before admission	3.89	.02
Albumin (per 1 g/dL increase)	3.12	.01

RICU = respiratory ICU

Discussion

In this study we have demonstrated for the first time that the patient's location prior to RICU admission profoundly influences outcomes, since the step-down subjects and those admitted from the emergency department had a better survival rate than the step-up subjects who had transited through a medical ward or respiratory ward. These latter subjects were also, on average, more severely ill than those transferred from an ICU or the emergency department, most likely because their conditions worsened while being outside of a "protected" environment.

In Europe, a RICU located inside an acute care hospital should admit patients suffering from acute or acute-on-chronic respiratory failure not immediately needing endotracheal intubation but requiring close monitoring, patients with single organ failure needing invasive ventilation, patients requiring NIV, and patients to be weaned from invasive mechanical ventilation.[1] In North America most of the intermediate care units accept a variety of patients, not just patients in respiratory failure,[12,13] so the results of this study may not be generalized, but may basically reflect a different international attitude.

These different conditions reflect different flows of patients once admitted to a general hospital. For example, in a survey conducted in 26 RICUs in Italy, Confalonieri et al[14] found that almost half the patients (47%) were admitted from emergency departments, 19% from other medical wards, 18% from ICUs, 13% from specialist respiratory wards, and 2% following surgery. This is perfectly in keeping with the data collected in our 7-bed RICU in a general hospital for about 1,400 patients and serving a population of 800,000 inhabitants.

Despite the fact that several investigations have assessed the outcomes of patients admitted to RICUs,[12-14] none has considered the effect of the admission pattern, which may serve to deliver step-down or step-up care or to admit directly from the emergency department.[15] The clinical outcome of patients requiring ICU admission (the step-down pattern) has been described in the recent literature, especially for the subset of patients requiring prolonged mechanical ventilation and transferred to a RICU located inside a rehabilitation center or long-term acute care hospital, which is increasingly utilized after a critical illness, especially in North America.[16,17] Data collected on more than 3,000 patients admitted to 5 Italian RICUs, mainly dedicated to weaning from mechanical ventilation, showed a mortality rate of about 15%,[18] which is in line with our results. Concerning a RICU located inside an acute care hospital, Bigatello et al[19] suggested that a considerable number of patients were ready to come off mechanical ventilation at the time of RICU admission, implying that in the preceding ICU stay, discontinuing mechanical ventilation had not always been a priority, and explaining the quite low mortality rate even 1 year after hospital admission.

The data obtained in the present study (~18% mortality) are in line with those from previous studies, and the deaths were homogenously distributed among patients from the 3 different ICUs of provenance. No differences were observed between the 2 main different locations prior to RICU admission. This is probably because the purpose of our RICU is to admit mainly "respiratory" patients, with single organ failure, so the characteristics of our transferred subjects were rather homogeneous. No subjects were admitted from the coronary care unit of our hospital, since this is organized in such a way that the staff take direct care of their patients, even when these need mechanical ventilation, or in the worst case they have a "preferential channel" with our post-transplant/ECMO ICU.

The mortality rate of the subjects from the emergency department was similar to that of the subjects from the ICUs. This may be explained by the these subjects' SAPS II, which was almost identical to that of the subjects from the ICUs, despite that the latter were mainly invasively ventilated, but in a phase of clinical stability. The subjects from the emergency department were "acutely" ill and undergoing an episode of acute respiratory failure. Interestingly, ~50% of this group of subjects were ventilated noninvasively; one could, therefore, have expected a better hospital survival, especially if the subjects were treated within a protected environment. However, not all the subjects were affected by acute hypercapnic respiratory failure, in which NIV is associated with the best outcome; in fact, some of the subjects had "pure" hypoxic respiratory failure, such as ARDS, in which NIV is associated with a higher failure rate and mortality.[20] Indeed, some subjects, mostly those who were very elderly and with several comorbidities, had DNI orders, so NIV was a ceiling treatment with a palliative aim to improve dyspnea.[21] In our study, NIV was a ceiling treatment in 41 (13%) of the total 326 subjects.

The most interesting finding of the present study is that the mortality rate in the step-up subjects (transferred to the RICU after having transited through a general or specific ward) was higher than in those admitted from other locations, with those coming from the respiratory ward having the higher risk of death.

The step-up subjects had higher SAPS II and were older, so it is not surprising that their mortality rate was also much higher than that of subjects with lower SAPS II transferred from an ICU or the emergency department. It may, therefore, be claimed that it is the severity of disease itself rather than the location that determines these patients' outcome.[22-24] Unfortunately, given the lack of a standardized database in all the units, we were unable to detect a progressive deterioration of clinical condition during the hospital stay. Simchen et al[25] demonstrated that about 2% of all patients admitted to the regular departments of an acute care hospital deteriorate during their hospital stay and reach the criteria of admission to a critical care environment. The majority of these patients (55%) were not, however, transferred early to the ICU or similar environment, so their mortality was likely to increase. Simchen et al concluded that prompt admission to a critical care environment in patients deteriorating while in hospital wards should be imperative to maximize survival, but that this occurred in only a small proportion of patients. This suggests that we should look carefully at patients admitted to wards with respiratory disease, in case we are mis-triaging some patients to lower levels of care than they truly need.

Another problem is the fact that intensivists (ie, those working in ICUs) are usually involved as "first-line call" for patients admitted to a medical ward, and that, due to the paucity of ICU beds, they often deny transfer for old patients or those with several comorbidities, since the physician's perception of poor prognosis is associated with less aggressive or invasive care. The paucity of beds is a limiting factor for access to a general ICU, at least in most European countries. The decision to admit a patient to this setting has been reported to be influenced by the physician's perception of prognosis, which has been shown to be overly pessimistic, with the risk of barring access to ICU to patients who may have a chance of surviving.[26] Other studies from different countries have confirmed the existence of this trend, indicating that intensivists are very selective in allowing transfer to the ICU.[27,28] Specialized ICUs such as RICUs may provide an alternative for the referral of patients who develop severe respiratory failure in a regular medical ward, but RICUs are generally present only in large hospitals, and, even when available, ward physicians tend to consult first with the general intensivists.

RICUs usually care for older, chronically ill patients, so it is likely that the higher mortality in patients admitted from the wards may simply reflect the fact that some of these patients had end-stage diseases. This is a striking finding in the patients transferred from our respiratory ward; in 31% of these subjects NIV was a ceiling treatment. However, subjects with DNI orders were separated in the analysis from other patients undergoing NIV treatment; they were also evenly distributed across patients from the various different pre-RICU locations: 27% were from the respiratory ward, 19% from medical wards, 32% from the emergency department, and 22% from ICUs, so their inclusion in the analysis does not alter the finding that pre-RICU location affects prognosis.

The present study confirms most of the previous findings of other investigators in the same setting, for example, that albumin level and age are predictors of hospital mortality. Malnutrition associated with advanced lung disease has been termed the "pulmonary cachexia syndrome": it is associated with an accelerated decline in functional status and is recognized as an independent predictor of mortality in patients with lung diseases.[22]

In the univariate analysis the use of NIV was associated with an increased risk of mortality, which was a surprising finding since NIV improves survival, compared to standard medical treatment, at least in patients with acute hypercapnic respiratory failure.[29] It should, however, be noted, as previously stated, that NIV was used in the RICU in some cases (in patients with DNI orders) as a palliative tool. Moreover, NIV was also used in patients with hypoxic respiratory failure, including those with pneumonia. Both these circumstances affect the perceived success of NIV in this study. Indeed, it is our policy to treat all patients with a COPD exacerbation with respiratory failure and a pH $>$ 7.25 in the respiratory ward.[30]

Only a small proportion of our patients were discharged to home from the RICU, in line with data reported by Bigatello et al,[19] who reported that only 2% of their patients were discharged to home.

Interestingly, we also confirmed that RICU admission is associated with a quite high rate of weaning from mechanical ventilation, since the percentage of patients invasively ventilated at discharge decreased from 70% to 40%.

The present study has some biases. The first and probably most important is that the data were collected in a single RICU in an acute care hospital, and the results, therefore, may not be extrapolated to other hospitals and geographic locations. Second, almost all the patients had been admitted for medical problems, while only 3 were post-surgery patients, and they are therefore representative of only one part of the population admitted to a critical care environment. Lastly, as previously stated, it was often difficult to collect a complete clinical history (in particular, previous lung function data), especially from patients transferred from a medical ward, since these patients were often in critical condition on RICU admission.

Conclusions

We have shown that the pathway of admission to a RICU is one of the major determinants of outcome. Step-up patients, transferred because of clinical deterioration, from a medical or respiratory ward are more severely ill and therefore more likely to die. Age, female sex, and nutritional status were also major determinants of survival. The use of NIV in the RICU is often not curative but only palliative.

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