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Outcome after acute respiratory failure is more dependent on dysfunction in other vital organs than on the severity of the respiratory failure

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Abstract

Introduction The incidence and outcome of acute respiratory failure (ARF) depend on dysfunction in other organs. As a result, reported mortality in patients with ARF is derived from a mixed group of patients with different degrees of multiorgan failure. The main goal of the present study was to investigate patient outcome in single organ ARF.

Patients and method From 1 January 2000 to 1 July 2002, all adult patients (>16 years) in the intensive care unit (ICU) at Haukeland University Hospital were scored daily using the Sequential Organ Failure Assessment (SOFA) score for organ failure. ARF was defined by the SOFA criteria: ratio of arterial oxygen tension to fractional inspired oxygen, with a value <26.6 kPa (200 mmHg) in more than one recording during the ICU stay (SOFA score 3 or 4). Patients with ARF alone and in combination with other severe organ failure (SOFA score 3 or 4) were included. Survival was recorded on discharge from the ICU, at hospital discharge and at 90 days after ICU discharge.

Results During the period of study, 832 adult patients were treated and 529 (63.0%) had ARF. The ICU, hospital and 3-month mortality rates were lowest in single organ ARF (3.2, 14.7 and 21.8%, respectively), with increasing mortality with each additional organ failure. When ARF occurred with four or five additional organ failures, the 3-month mortality rate was 75%. No significant differences in mortality were found between early and late ARF.

Conclusion The prognosis for ICU patients with single organ ARF is good, both in the short and long terms. The high overall mortality rate observed is caused by dysfunction in other organs.

Keywords acute respiratory failure, intensive care, organ failure, outcome, Sequential Organ Failure Assessment, survival

Introduction

Acute respiratory failure (ARF) is the most common organ failure in a general intensive care unit (ICU), and the mortality rate is high. In a recent epidemiological study conducted in Scandinavia, the 90-day mortality rate in ARF patients was similar to those in acute respiratory distress syndrome

ALI = acute lung injury; ARDS = acute respiratory distress syndrome; ARF = acute respiratory failure; CI = confidence interval; FiO_2 = fractional inspired oxygen; ICU = intensive care unit; MODS = multiple organ dysfunction score; PaO_2 = arterial oxygen tension; SAPS II = Simplified Acute Physiology Score version 2; SOFA = Sequential Organ Failure Assessment.

(ARDS) and acute lung injury (ALI), namely 41.0% and 42.2%, respectively [1]. ARF is often followed by failure in other vital organs, and death more often occurs because of multiple organ dysfunction syndrome (MODS). Even in ARDS, irreversible respiratory failure is responsible for only 10–16% of the deaths [2,3]. It is thus difficult to separate the mortality rate from ARF alone from death caused by MODS.

The present study was performed to evaluate the outcome of ARF with and without concomitant failure in other vital organs.

Patients and method

The study was prospective and based on daily registration of data from the 10-bed mixed ICU at the Haukeland University Hospital. Burns patients, post-cardiac surgery patients, and patients primarily with cardiac disorders are treated in separate dedicated units, and were not included in the study. Patients older than 16 years, admitted from 1 January 2000 to 1 July 2002 (30 months), were included.

There are 400–450 ICU admissions to this ICU each year, and since 1994 relevant clinical data have been gathered in the ICU database Regina [4]. On admission to the ICU patients were categorized into one of eight primary intake groups (respiratory, circulatory, gastrointestinal, renal, neurological, postoperative, multitrauma and miscellaneous). All patients were registered with the Simplified Acute Physiology Score version 2 (SAPS II) [5] after 24 hours in the ICU. Diagnoses according to the International Classification of Diseases version 10 [6], ICU procedures, duration of stay and ventilator time were recorded.

Organ failure assessment

In order to assess the occurrence of vital organ failure, the Sequential Organ Failure Assessment (SOFA) score was used [7]. Clinical and biochemical data were retrieved manually from the ICU records and transferred to a dedicated SOFA record form. Data were recorded daily at 0800 hours by all ICU physicians, and the worst registration for each parameter from the previous 24-hour period was used. When the patients were discharged from the ICU, data were entered into the clinical database by one of the ICU physicians (HF) and processed using the equations for the SOFA score. For a single missing value (most often thrombocytes and bilirubin), a value for that parameter was calculated using the mean value of the results on either side of the absent result. When there was no obvious central nervous system dysfunction or cerebral pathology, the Glasgow Coma Scale score was set to 15 (normal).

Definition of acute respiratory failure

The definition of ARF was based on the SOFA score criteria, in which a score of 3 or 4 is defined as 'severe' organ failure [8]. According to those criteria, the diagnosis of respiratory failure is based on the ratio of arterial oxygen tension (Pa_{O_2}) to fractional inspired oxygen (Fi_{O_2}). A ratio from 13.3 to 26.6 kPa (100–200 mmHg) and a ratio below 13.3 kPa (<100 mmHg) yield SOFA scores of 3 and 4, respectively. In order for a SOFA score greater than 2 to be recorded, the patient additionally had to receive ventilatory support, including all methods of artificial ventilation, with or without the presence of an artificial airway.

Study groups

The main study group included patients with single organ severe ARF (SOFA score 3 or 4) without concomitant severe organ failure (SOFA score 0 to 2) during the ICU stay. We also studied patients in whom severe ARF was complicated by an increasing number of other vital organs in severe failure (SOFA score 3 or 4) during the ICU stay. Because of the small number of patients, no further subdivisions of ARF and selected organ failure were evaluated. This left us with six groups of patients: those with ARF alone, and those with one to five additional organ failures.

Outcome

The ICU, hospital and 90-day mortality rates were routinely recorded in all of the ICU patients. The hospital mortality rate was retrieved from the hospital patient management system, and the 90-day mortality rate was attained from the Peoples Registry of Norway, in which all deaths are recorded within 14 days after the death certificate has been issued. Patient outcome was further stratified using the SOFA score.

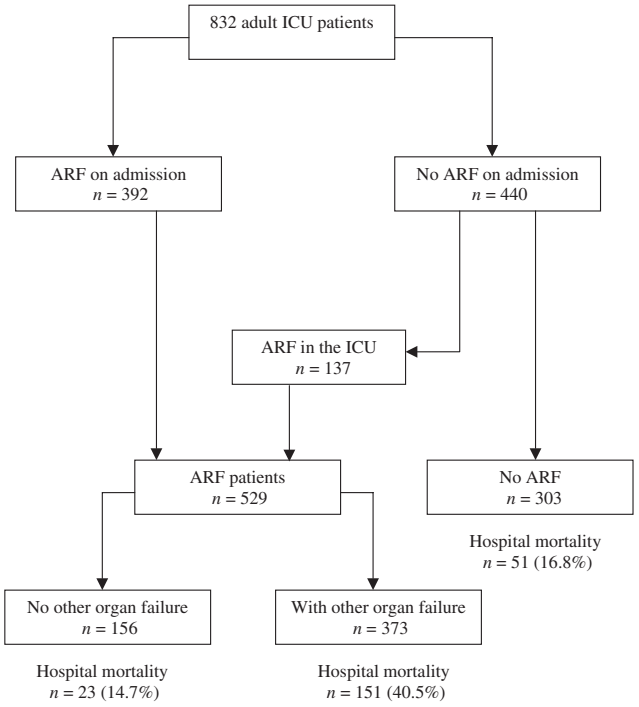
Statistics

Three-month mortality rate was analyzed using Kaplan–Meier survival statistics. Otherwise, 95% confidence interval (CI) was calculated to identify differences between numbers and means. When the 95% CI of differences excluded 0, this was interpreted as a significant difference between the compared numbers. The *t*-test was also used to compare differences in daily Pa_{O_2}/Fi_{O_2} ratio. The log rank (Mantel–Cox) test was used to test differences in survival, and $P < 0.05$ was considered statistically significant. Standardized mortality ratio was calculated as the ratio between the observed SAPS II score and predicted mortality rate. SPSS version 11 for Windows (SPSS Inc., Chicago, IL, USA) was used in statistical calculations.

Results

During the 2.5-year study period (1 January 2000 to 1 July 2002), 946 patients were admitted to the ICU, with 1032 ICU stays. Of those patients, 832 were older than 16 years. The main study groups are illustrated in Fig. 1. Patients were divided in three categories: 1, unscheduled surgery; 2, scheduled surgery; or 3, medical according to the SAPS II definitions. ARF was diagnosed in 529 patients (63.0%), with 585 ICU admissions. The distribution of patients in the six subgroups with increasing number of additional organ failures is shown in Table 1. Multitrauma was the main reason for ICU admission in 60 (11.3%) of these patients.

Figure 1



The main study groups shown as a flowchart, with the number and hospital mortality rates shown for each group.

The total ICU stay was 3241 days. The SOFA score was missing in 488 days, mainly on the discharge day for ICU survivors (410 days).

The ICU, hospital and 90-day mortality rates were lowest in the subgroup with ARF as a single organ failure (3.2, 14.7 and 21.8%, respectively), and they gradually increased with the number of additional organs in failure (Table 1). Within the group of patients with single ARF failure ($n = 156$), 132 had a maximum ARF SOFA score of 3 and 24 had a maximum SOFA score of 4, with 90-day mortality rates of 20.5% and 29.2%, respectively (difference 8.7%, 95% CI −10.7% to +28.2%). Overall ICU, hospital and 90-day mortality rates in the whole group with ARF ($n = 529$) were 22.1, 32.9 and 45.4%, respectively. The SAPS II estimated mortality rate (hospital mortality rate) was 37.4%, yielding a standardized mortality ratio of 0.77 versus a ratio of 0.78 for the whole ICU population ($n = 840$) older than 16 years. The 90 days Kaplan–Meier survival curves are shown in Fig. 2.

Of all patients with ARF 392 had severe respiratory failure at admission, whereas in 137 ARF was diagnosed during the ICU stay (Table 2). There were no significant differences in 90-day mortality between these two groups (difference 5.1%, 95% CI −4.5% to +14.7%).

At admission a subgroup patients with ARF ($n = 137$) presented with single organ ARF and 254 patients had one or more additional organs in severe failure (SOFA score 3 or 4). Mortality was higher in the group presenting with more than one organ in failure at admission (Table 2). The difference in 90-day mortality was 35.7% (95% CI 26.4% to 45.0%).

Patients with single organ ARF had a mean PaO_2/FiO_2 ratio during the first 24 hours in the ICU of 22.3 kPa, whereas patients with ARF and other severe organ failure had a mean ratio of 19.9 kPa. Evolution of the PaO_2/FiO_2 ratio from ICU days 1–10 is given in Fig. 3. The mean oxygen ratio on days 1–4 was significantly different between patients with ARF as a single organ failure and those with MODS ($P < 0.01$).

The main diagnoses in patients with single organ ARF dying in hospital after ICU discharge were malignancies (12 patients), amyotrophic lateral sclerosis (2 patients) and

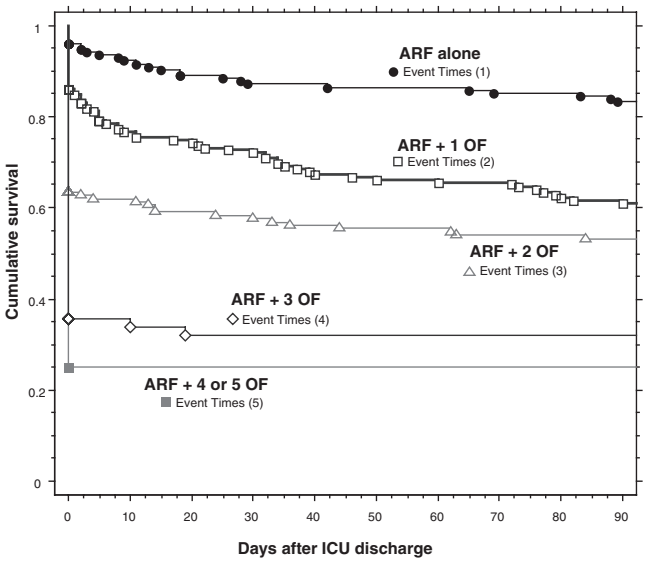
Table 1

Severity of illness and outcome in the six study groups of acute respiratory failure with increasing number of additional organs in failure

				Mortality (*n* [%])		
Group	*n*	Age (years [mean])	SAPS II (mean)	ICU	Hospital	90-day
ARF + 0	156	57.8	33.0	5 (3.2)	23 (14.7)	34 (21.8)
ARF + 1	172	61.6	45.8	20 (11.6)	49 (28.5)	75 (43.6)
ARF + 2	137	53.2	54.5	48 (35.0)	57 (41.6)	78 (56.9)
ARF + 3	56	56.7	62.0	38 (67.6)	39 (69.6)	46 (82.1)
ARF + 4/5	8	58.4	70.4	6 (75.0)	6 (75.0)	7 (87.5)
ARF + any*	373	57.7	52.0	112 (30.0)	151 (40.5)	175 (46.9)
ARF all	529	57.7	46.4	117 (22.1)	174 (32.9)	201 (38.0)

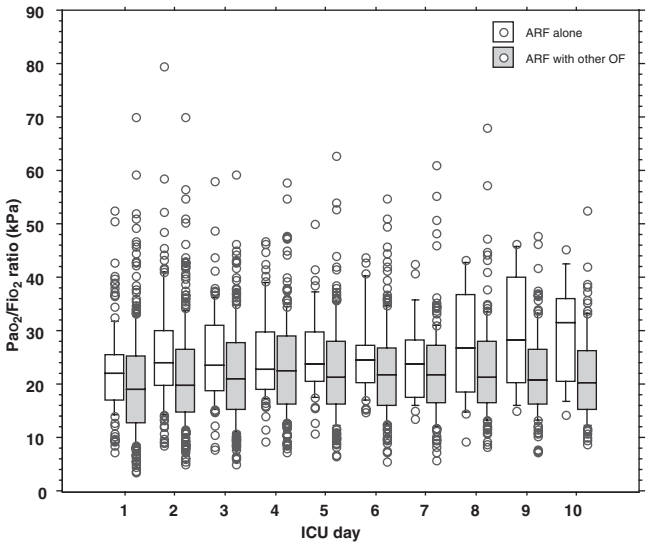
The two groups with four ($n = 6$) and five ($n = 2$) organs in failure are merged because of the small number of patients. *Any combination of acute respiratory failure (ARF) and other severe organ failure. SAPS II, Simplified Acute Physiology Score version 2.

Figure 2



Kaplan–Meier survival analysis after intensive care unit (ICU) discharge in five groups of patients with acute respiratory failure (ARF). Patients dying in the ICU are represented with survival = 0. OF, organ failure.

Figure 3



Arterial oxygen tension/fractional inspired oxygen (PaO_2/FiO_2) ratio (kPa) shown as box plot with median values and interquartile range in the two groups of patients with acute respiratory failure (ARF) alone and ARF with other organ failure during their hospital stay (from days 1–10).

various reasons (6 patients: chronic renal failure/renal transplantation, alcoholic liver cirrhosis, small bowel infarction, ruptured thoracic aortic aneurysm, subarachnoid haemorrhage and peritonitis).

Discussion

The data presented here show that patients with at least 1 day of respiratory failure (SOFA score 3 or 4) without any other severe organ failure had a hospital mortality rate of 14.7%. In contrast, all ARF patients, regardless of other concomitant organ failure, had an overall hospital mortality of 32.9%. The mortality increased with the additional number of organs in failure. There was no difference in mortality between those with severe ARF at admission and those in whom ARF developed at other time points during the ICU stay.

There are several methods with which to assess organ failure, the most commonly used in general ICU patients being SOFA score [5], Multiple Organ Dysfunction Score [9] and Logistic Organ Dysfunction [10]. Scores derived from SOFA, such as Total Maximum SOFA score and delta SOFA score, have also been used to assess outcome [11–13]. Comparisons of these three organ dysfunction scoring systems have shown that all are reliable outcome predictors [14–16] and are comparable to and even better than traditional outcome scoring systems [12,16,17]. In addition, the SOFA score has been shown to be a reliable marker of organ dysfunction in

Table 2

Patients with acute respiratory failure diagnosed during intensive care unit stay

				Mortality (*n* [%])		
Group	*n*	Age (years [mean])	SAPS II (mean)	ICU	Hospital	90-day
A	392	58.6	46.9	22.6	34.2	46.7
D	137	55.2	43.0	19.0	29.2	41.6
A1	137	59.6	35.7	4.4	18.2	23.4
A2	255	58.2	53.9	33.1	42.5	59.1

Group A had acute respiratory failure (ARF) at admission; group D developed ARF during the intensive care unit (ICU) stay. Group A is further subdivided into patients with single organ ARF at admission (A1) and ARF with other organ failure at admission (A2). SAPS II, Simplified Acute Physiology Score version 2.

subgroups of ICU patients such as those with acute pancreatitis [17], peritonitis [18], liver cirrhosis [19], cardiovascular disease [12], trauma [20] and ARF [21].

Multiple organ failure is the most common cause of death in the ICU. The majority of such patients also have severe ARF, and often ALI or ARDS. The mortality rate in severe respiratory failure is therefore often caused by combined organ failure, and not attributable to just a single severe organ dysfunction. This is acknowledged, but few studies have reported mortality data for subgroups of patients with single organ failure when investigating outcome after ARF. An international prospective study using the SOFA score [8] reported ICU mortality data for patients with individual organ failure alone and in combination with other organ failures. In that study, ARF occurred only in 241 patients (16.6% of all patients), with an attendant mortality of 20.7%. The combination of ARF with cardiovascular, renal or neurological failure was associated with mortality rates of 55.4, 57.4 and 48.1%, respectively.

In a large ARF incidence study from Scandinavia, Luhr and coworkers [1] found an overall 90-day mortality rate among patients with ARF of 41.0%, with no significant difference between patients with ALI or ARDS (42.2% and 41.2%, respectively). The definition of ARF used by those investigators was slightly different from that used in the present study, because they included all patients who were intubated and ventilated (for more than 24 hours), regardless of FiO_2 and hence oxygen ratio. They made no attempt to adjust mortality data for dysfunction in other vital organs, and hence their data cannot be used to evaluate mortality following ARF alone. In a recent international study of patients receiving mechanical ventilation irrespective of their oxygen ratio [22], the overall ICU mortality was found to be 31%. The mortality rate was found to be more than doubled when shock, renal failure, coagulopathy, hepatic failure or ARDS was superimposed.

Our definition of ARF using SOFA score criteria is closer to the definitions reported from the American–European Consensus Conference on ARDS [23], with an acute onset and an oxygen ratio below 26.6 kPa (200 mmHg). Because of the lack of information concerning chest radiograph and left ventricular function, we cannot strictly define all our patients as having ALI or ARDS, although the oxygen ratio in our patients was on the same level as that in ARDS patients.

Our data demonstrate that the PaO_2/FiO_2 ratio evolved similarly during the first week in the ICU in all patients with ARF, regardless of concomitant organ failure. After 7 days the groups diverged, with no further rise in the oxygen ratio in ARF complicated by other organ failure, whereas there was an increase in patients with single organ ARF. However, these changes were not significant because of the small number of patients staying more than 1 week in the ICU. Likewise, we could not find any differences in outcome depending on the time of first occurrence of ARF.

Key messages

- ARF is the most common organ failure seen in the ICU, and was present in 63.0% of patients older than 16 years
- Severe ARF without other severe organ failure had a comparatively low mortality rate, with ICU, hospital and 3-month mortality rates of 3.2, 14.7 and 21.8%, respectively
- When severe respiratory failure is accompanied by other severe organ failure, the mortality increased depending on the number of organs in failure, and reached 75% in the group with five or six severe organ failures

The total incidence of severe ARF in this study was 63%, which is a little higher than the 56% found in a recent European survey using the same SOFA criteria [24]. In that study an overall ICU mortality of 31% was found in ARF patients, regardless of the presence of other organ failure, and when the lungs were the only organ in failure (275 patients, 20% of the patient population) the ICU mortality was 7%. Case-mix was not very different from that in the present study, but non-operative patients comprised 44% of that sample versus 32% in our study. No data were given on the number of emergency surgical admissions. Interestingly, only five (3.2%) of our ARF patients with single organ failure died in the ICU, whereas 18 (11.5%) died on the wards, making the overall hospital mortality rate 14.7%. All patients dying on the ward had severe underlying diseases such as disseminated cancer (60%) or amyotrophic lateral sclerosis.

The low mortality associated with ARF when it presented as a single organ failure was recently documented in a study from Finland [16], which compared the use of different scoring systems for multiple organ dysfunction. The investigators found the frequency of ARF using the SOFA criteria to be 169/520 (32.5%), with an overall hospital mortality rate of 46%. In those patients with single organ ARF (only 24 patients) the hospital mortality rate was 17%, which is very similar to our findings. In that study, the incidence of ARF was lower than that in the European multicentre study and in our patients, but the overall mortality rate in patients with ARF was higher. One explanation may be the differences in case-mix, because the number of medical admissions was more than twice that in the present study (66%).

Conclusion

We found that a large group (156/840, 18.6%) of adult ICU patients had ARF without other severe organ failure. In these patients ICU, hospital and 3-month mortality rates are comparatively low, representing a good prognosis for this subgroup of patients. The hospital and 90-day mortality rates approximately doubled when one more organ failure occurred during ICU stay.

Our data confirm that, in general, the outcome of patients with ARF mostly depends on concomitant occurrence of other severe organ failure. Hospital mortality in patients with single organ ARF appears to be more related to the underlying disease process (e.g. cancer or amyotrophic lateral sclerosis) than to the severity of ARF.

Competing interests

None declared.

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