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Quality of life in acute respiratory distress syndrome survivors may be no worst than in other ICU survivors

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Abstract *Objective:* To compare the health-related quality of life (HR-QOL) in acute respiratory distress syndrome (ARDS) survivors with that in a matched control group of non-ARDS survivors. *Design and setting:* Prospective, matched, parallel cohort study, comparing HR-QOL between intensive care unit (ICU) survivors with ARDS and a control group in a tertiary care hospital. *Patients:* Between May 1997 and December 2000, all ARDS adult patients of an eight-bed medical/surgical unit of a tertiary care hospital were enrolled and a control group of non-ARDS survivors, matched for severity of disease and for previous health state, was selected. The study included 29 ARDS survivors who answered the EQ-5D questionnaire and had lung function evaluated. *Measurements and results:* A follow-up appointment was performed 6 months after ICU discharge consisting of: (a) evaluation of HR-QOL using EQ-5D and (b) lung function tests and measure of diffusing capacity. Among ARDS survivors 41% had normal lung function and 59% mild to moderate lung function impairments. Nearly a one-third of ARDS survivors reported problems in one or more of the five dimensions of the EQ-5D, and 48% reported feeling worse at the interview than 6 month before ICU admission. No significant differences were found in HR-QOL between ARDS survivors and other ICU survivors with similar age and matched for previous health state and severity of disease. *Conclusions:* This study suggests that impairments in HR-QOL among ARDS survivors may not be distinguishable from that among other ICU survivors.

Keywords Acute respiratory distress syndrome · Quality of life · Health-related quality of life · EQ-5D questionnaire · Lung function recovery · Outcome

Introduction

The acute respiratory distress syndrome (ARDS) is a rapidly progressive illness associated with high morbidity and mortality which requires aggressive therapy and advanced technological support. Recent reports suggest that the mortality rate has declined, but it still ranges between 34% and 60% [1, 2]. Consequently the main concerns relating to ARDS patients have been ways of improving survival. More recent outcome studies have documented residual pulmonary dysfunction after ARDS [3, 4, 5]. Health-related quality of life (HR-QOL) has also been studied, with most authors reporting lower HR-QOL in ARDS survivors than in the normal population [5, 6, 7, 8, 9]. Moreover, reductions in HR-QOL of ARDS survivors compared with critically ill controls have also been suggested by one study [10].

A number of factors make HR-QOL evaluation difficult: (a) those related to the HR-QOL evaluation in general, such as the timing of data collection, the choice of

particular dimensions to be included, and the lack of consensus over the instruments to be used; (b) those related to HR-QOL specifically after ARDS, such as the lack of an appropriate comparison group, the lack of previous HR-QOL evaluation [10, 11], the extent to which ARDS sequelae influence HR-QOL. The cost-effectiveness of the treatment in ARDS patients has also been studied [11, 12].

The aim of this study was to compare HR-QOL in ARDS survivors with that in similar ICU survivors, using a control group without ARDS and matched by previous health state and severity of disease.

Patients and methods

The study addressed all adult patients (18 years old or more) admitted to an eight-bed medical/surgical ICU between May 1997 and December 2000 in whom ARDS was diagnosed according to the criteria of the American-European Consensus Conference on ARDS: acute onset: PaO_2 of 200 mmHg or lower; bilateral infiltrates on frontal chest radiograph, Paw of 18 mmHg or lower, or no clinical evidence of left atrial hypertension [13]. Survivors with previous chronic lung disease (chronic bronchitis and emphysema) were excluded.

Background variables included patient's gender, age, main activity, smoking habits, and previous (i.e., premorbid) health status. Previous health status was evaluated according to three categories: healthy, chronic nondisabling diseases (i.e., able to keep work or normal daily activities) and chronic disabling diseases (i.e., unable to work or to undertake normal daily activities). One of the authors classified all patients according to one of these three categories. ICU variables included severity of disease at admission, length of stay and diagnosis. ARDS variables included primary or secondary pulmonary lesion, days of ventilation, lung injury score, maximum values of positive end-expiratory pressure (PEEP), and the number of days with a FIO_2 greater than 60%.

From a total of 1251 patients, 88 with the diagnosis of ARDS were enrolled in the study; 26 of these died in the ICU and another 7 in the ward (38% in-hospital mortality rate). Three patients died after hospital discharge but before the 6-month evaluation. Nine patients were excluded for previous chronic lung disease, and another 14 were lost to follow-up (i.e., nonrespondents; Table 1). A follow-up appointment was performed 6 months after ICU discharge consisting of an evaluation of HR-QOL using EQ-5D [14], lung function tests, and measure of diffusing capacity (DLCO). DLCO was measured by the single-breath carbon monoxide technique. SensorMedics Vmax22 was the pulmonary system used. Recommendations for standard technique (ATS update 1995) were followed. Six months after ICU discharge 29 patients completed EQ-5D questionnaire and had their lung function evaluated. The most frequent diagnoses were pneumonia (*n*=13), sepsis (*n*=7), aspiration (*n*=2), multiple trauma (*n*=2), and intoxication (*n*=2).

HR-QOL was measured using EQ-5D questionnaire. This is a generic measure instrument designed to measure health outcome, which was developed at a European level [14, 15]. The EuroQol Group originally developed the Portuguese version of the EQ-5D in 1998 (EuroQol Group Newsletter, January 2000). The EQ-5D comprises two parts: the EQ-5D self-classifier, a self-reported description of health problems according to a five dimensional classification i.e., mobility, self-care, usual activities, pain/discomfort and anxiety/depression (see Table 5 for description of the EQ-5D self-classifier); the EQ visual analogue scale (VAS), a self-rated health status of a form similar to a thermometer to record perceptions of participants own current overall health; the scale is graded

Table 1 Characteristics of nonsurvivors and survivors of ARDS. Statistically significant differences were found between ARDS nonsurvivors and survivors in age, APACHE II at admission, and lung injury score; and between ARDS respondents and nonrespondents in ICU days and days of ventilation (*P5–P95* 5th–95th percentiles)

	Total (*n*=88)	ARDS nonsurvivors			ARDS survivors		
		In ICU (*n*=26, 30%)	In ward (*n*=7, 8%)	In first 6 months (*n*=3, 3%)	Respondents (*n*=29, 33%)	Non-respondents (*n*=14, 16%)	Excluded (*n*=9, 10%)
Gender							
Male	59 (67%)	20 (77%)	6 (86%)	0 (0)	18 (62%)	8 (57%)	7 (78%)
Female	29 (33%)	6 (23%)	1 (14%)	3 (100)	11 (38%)	6 (43%)	2 (22%)
Age, median (P5–P95)	48 (24–79)	60 (22–84)	63 (37–78)	49 (37–76)	45 (24–72)	53 (16–88)	35 (26–67)
APACHE II at admission, median (P5–P95)	18 (7–33)	20 (9–45)	18 (9–33)	18 (16–23)	15 (5–28)	18 (5–26)	15 (5–25)
ICU days, median (P5–P95)	11 (2–63)	13 (1–77)	10 (2–32)	9 (3–52)	13 (4–89)	9 (3–39)	10 (4–41)
Diagnosis							
Medical	60 (68%)	17 (65%)	4 (57%)	1 (33%)	22 (76%)	10 (72%)	6 (67%)
Nonscheduled surgery	17 (19%)	5 (19%)	1 (14%)	2 (67%)	5 (17%)	2 (14%)	2 (22%)
Scheduled surgery	6 (7)	3 (12%)	2 (29%)	0 (0)	0 (0)	0 (0)	1 (11%)
Multiple trauma	5 (6)	1 (4)	0 (0)	0 (0)	2 (7)	2 (14%)	0 (0)
Pulmonary lesion							
Primary	59 (67%)	18 (69%)	4 (57%)	1 (33%)	19 (66%)	11 (79%)	6 (67%)
Secondary	29 (33%)	8 (31%)	3 (43%)	2 (67%)	10 (34%)	3 (21%)	3 (33%)
Days of ventilation, median (P5–P95)	9 (3–51)	12 (2–79)	14 (2–30)	8 (3–50)	11 (3–66)	5 (2–35)	9 (3–41)
Lung injury score, median (P5–P95)	2.50 (1.75–3.50)	2.75 (1.75–3.66)	2.75 (2.25–3.00)	3.00 (2.50–3.25)	2.50 (1.38–3.75)	2.25 (1.75–3.25)	2.00 (1.75–3.00)

from 0 (the worst imaginable health state) to 100 (the best imaginable state) [15] (EuroQol Group Newsletter, January 2000). In both the time frame is the current day. Because the ICU stay was only 6 months before the interview, the "perceived current health status" asked in the EQ-5D questionnaire was changed from "compared with my general level of health over the past 12 months my health state today is better/the same/worse" to "compared with my general level of health 12 months ago my health state today is better/the same/worse." An index (EQ Index), based on the five dimensions and the EQ VAS and ranging from 0 to 100 was also calculated and used to describe the overall QOL of these patients [16, 17].

All questionnaires were administered by one of the authors during a follow-up consultation 6 months after ICU discharge. A matched control group was created, with two controls for each survivor of ARDS, with the same previous health state and similar Acute Physiology and Chronic Health Evaluation (APACHE) II (±2 units), which were randomly selected among other ICU survivors without the diagnosis of ARDS. Scheduled surgery patients were excluded from controls, as there were no scheduled surgery patients among ARDS respondents.

Pearson's χ^2 test was used for analysis of categorical data, and the Mann-Whitney test was used for continuous variables with asymmetrical distribution. Friedman's test for matched ordinal data was used to compare EQ-5D dimensions and the paired sample *t* test to compare EQ VAS and EQ Index dimensions between ARDS group and the two paired control groups. Statistical significance was set at $p<0.05$. The hospital's ethics committee approved the study.

Results

There were significant differences between survivors and nonsurvivors concerning background variables with the latter being significantly older than the former. Concerning ICU variables, we found significant differences in severity of disease, as those who died had more severe disease, as measured by APACHE II. We also found differences in ARDS variables, as the lung injury score was significantly higher in nonsurvivors. There were no significant differences between respondents and nonrespondents except in the time of ventilation and ICU length of stay (Table 1). Differences between respondents and nonrespondents in the control group were not explored as we have previously found that there were no differences in a group including all patients admitted in the ICU [18].

Of the 29 survivors 17 exhibited abnormalities in lung function (Table 2). Lung function impairments were mild to moderate, and many patients had impairments only in carbon monoxide diffusion. There were no significant differences between those survivors with normal lung function and those with residual pulmonary dysfunction, either in background variables, ICU variables, or ARDS variables. Patients with impairments in lung function

Table 2 Lung function in ARDS survivors (*FVC* forced vital capacity, *FVE_1* forced expired volume in 1st second, *DLCO* diffusing capacity for carbon monoxide, *P5–P95* 5th–95th percentiles)

Patient no.	Smoker	FVC (%)	FVE_1 (%)	FVE_1 to FVC ratio (%)	DLCO (%)	Lung function
1	No	80	81	86	79	Impaired
2	No	50	62	91	–	Impaired
3	No	106	97	80	72	Impaired
4	No	113	82	62	76	Impaired
5	No	59	60	86	28	Impaired
6	No	113	109	78	48	Impaired
7	No	80	79	84	76	Impaired
8	No	67	76	92	–	Impaired
9	No	69	64	79	77	Impaired
10	No	120	117	79	70	Impaired
11	No	67	71	86	–	Impaired
12	No	125	111	69	78	Impaired
13	Yes	134	124	76	97	Impaired
14	Yes	97	76	63	91	Impaired
15	Yes	67	73	91	78	Impaired
16	Yes	114	94	68	70	Impaired
17	Yes	129	116	74	56	Impaired
18	No	102	117	94	116	Normal
19	No	112	117	81	120	Normal
20	No	127	127	81	97	Normal
21	No	94	94	84	86	Normal
22	No	132	136	89	103	Normal
23	No	105	105	88	86	Normal
24	No	97	104	93	–	Normal
25	No	114	102	75	–	Normal
26	No	95	89	80	–	Normal
27	No	111	117	91	105	Normal
28	No	112	102	79	109	Normal
29	No	86	90	89	87	Normal

Table 3 Comparison of ARDS survivors with normal and impaired lung function (*PEEP* positive end-expiratory pressure FIO_2 fraction of inspired oxygen, *no. days* $FIO_2 \geq 60\%$ number of days with a FIO_2 equal to or greater than 60%)

	Normal (*n*=12, 41%)	Impaired (*n*=17, 59%)	*p*
Gender			0.057[a]
Male	5 (42%)	13 (77%)	
Female	7 (58%)	4 (23%)	
Age, median (P5–P95)	42 (23–72)	51 (31–72)	0.152[b]
APACHE II at admission, median (P5–P95)	18 (8–29)	13 (4–26)	0.080[b]
ICU days, median (P5–P95)	12 (7–21)	21 (4–89)	0.080[b]
Diagnosis			0.457[a]
Medical	10 (83%)	12 (71%)	
Nonscheduled surgery	2 (17%)	3 (17%)	
Scheduled surgery	0	0	
Multiple trauma	0	2 (12%)	
Pulmonary lesion			0.494[a]
Primary	7 (58%)	12 (71%)	
Secondary	5 (42%)	3 (29%)	
Days of ventilation, median (P5–P95)	8 (3–18)	15 (3–70)	0.100[b]
Lung injury score, median (P5–P95)	2.63 (1.75–3.75)	2.50 (1.25–3.25)	0.419[b]
PEEP maximum, median (P5–P95)	8 (5–17)	8 (0–18)	0.159[b]
No. days $FIO_2 \geq 60\%$, median (P5–P95)	0 (0–4)	2 (0–14)	0.118[b]

[a] Pearson's χ^2 test
[b] Mann-Whitney *U* test

Table 4 Comparison of ARDS survivors with the control group: background and ICU variables

	ARDS survivors (*n*=29)	Control group (*n*=58)	*p*
Gender: M/F (%)	62/38	57/43	0.644[a]
Age, median (years)	45	59	0.216[b]
Occupation (%)			
Employed	39	18	0.159[a]
Retired	32	50	
Housework, student, unemployed	15	18	
Not returned to activity	14	14	
Smoking habits (%)			
Smoker	18	10	0.414[a]
Former smoker	50	44	
Never smoked	32	46	
Previous health status (%)			
Healthy	62	62	1.000[a]
Chronic nondisabling disease, chronic disabling disease	38	38	
APACHE II at admission, median	15	15	0.698[b]
ICU days, median	13	4	<0.001[b]
Diagnosis (%)			
Medical	76	60	0.171[a]
Nonscheduled surgery	17	36	
Multiple trauma		7	4

[a] Pearson's χ^2 test
[b] Mann-Whitney *U* test

were older, had a longer ventilation time, stayed longer in the ICU, and needed a FIO_2 greater than 60% for more days than survivors with normal lung function (Table 3). However, as none of these differences were statistically significant, we decided to analyze together these patients regarding their HR-QOL.

There were no differences between ARDS survivors and the matched control group concerning background variables (gender, age, main activity, smoking habits, and previous health state). Concerning ICU variables we found a significantly longer ICU stay in ARDS survivors (Table 4).

No significant differences were found in HR-QOL when evaluated by EQ-5D between ARDS survivors and other ICU survivors (control group; Table 5). Concerning the five dimensions, and except for anxiety/depres-

Table 5 Comparison of ARDS survivors with the control group: EQ-5D variables

	ARDS survivors (n=29)	Control group (n=58)	p
Mobility (%)			0.174[e]
No problems	86	69	
Moderate problems	14	26	
Extreme problems	0	5	
Self-care (%)			0.302[e]
No problems	86	71	
Moderate problems	7	16	
Extreme problems	7	14	
Usual activities (%)			0.471[e]
No problems	62	59	
Moderate problems	31	24	
Extreme problems	7	17	
Pain, discomfort (%)			0.491[e]
No problems	79	69	
Moderate problems	17	24	
Extreme problems	3	7	
Anxiety, depression (%)			0.210[e]
No problems	52	68	
Moderate problems	24	25	
Extreme problems	24	7	
Health state today vs. 1 year ago[a] (%)			0.302[e]
Better	24	30	
Same	28	40	
Worse	48	30	
EQ VAS, mean (1–100)	73	73[b,c]	0.991[f]
EQ Index, mean	82	79[b,d]	0.632[f]

[a] This question was modified from the original EQ-5D
[b] Mean score of the pair of controls
[c] Mean difference 0.1 (95% confidence interval of the difference −11.7 to 11.9)
[d] Mean difference 2.6 (95% confidence interval of the difference −8.3 to 13.4)
[e] Friedman's test
[f] Paired-samples t test

sion, there was even a trend for ARDS survivors to report fewer problems than the control group, although not reaching statistical significance. ARDS survivors reporting no problems in all five dimensions of the EQ-5D ranged from 52% for anxiety/depression to 86% for mobility and self-care; However, no other trend was observed, as there were no differences either in EQ VAS or EQ Index between the two groups. Concerning perceived current health state, 48% on the ARDS group and 30% in the control group claimed to be worse than 12 months previously (Table 5).

Discussion

This study found ARDS mortality to be significantly associated with age, severity of disease, and severity of ARDS. These findings agree with those of previous studies in which age [2, 19, 20] and lung injury score [2] were associated with mortality. Mild to moderate impairments in lung function have been previously described [3, 5, 7, 9], and we found a similar (approx. 60%) proportion of ARDS survivors with these impairments. Moreover, although not statistically significant, it was apparent that patients with impairments in lung function were older, had a longer ventilation time, stayed in the ICU longer, and needed FIO_2 greater than 60% for more days. These findings agree with those of McHugh et al. [3] who reported that improvement in lung function was related to a higher severity of lung injury and duration of ventilation. ARDS survivors also had a significantly longer median hospital stay, a finding similar to that of McHugh et al. [3], Davidson et al. [10] and more recently from Herridge et al. [5]. As in other reports [6, 7], we found a fair HR-QOL among ARDS survivors, although nearly one-third reported problems in at least one of the five dimensions of the EQ-5D.

To our knowledge, this is the first study using EQ-5D in a cohort of ARDS survivors. Together with SF-36, this instrument has been recently recommended as the best suited instrument to be used in critical care outcome studies [21]. The most striking finding in this study is that there were no differences in HR-QOL between ARDS survivors and a control group with similar age and matched for previous health state and severity of disease, which contrasts with a study from Davidson et al. [10]. However, some differences in the study design and methods may explain these conflicting results: our control group was matched for both severity of disease and previous health state, as these variables were found to be determinants of HR-QOL [18]. On the other hand, Davidson et al. [10] addressed a control group of critical patients matched for severity of disease and for diagnosis. Also, their study included only trauma and sepsis patients, patients with previous chronic lung disease were not excluded, and there is no information on their previous health status. Moreover, SF-36 was the generic questionnaire that was administered. More recently Herridge

et al. [5] drew our attention to the fact that the long-term effect of ARDS may be related to age and preexisting pulmonary function and may thus be cohort specific, which may help to explain different results between different studies.

This study presents some limitations. Firstly, we acknowledge the relatively small number of ARDS survivors involved and the consequent reduction in statistical power that could have prevented us from finding significant differences. However, it should be underlined that the differences in HR-QOL found between ARDS survivors and their controls were not only very small but also had an unexpected direction as ARDS survivors reported less moderate to extreme problems in most EQ-5D dimensions. Secondly, ARDS nonrespondents showed significantly shorter ICU stay and fewer days of ventilation regarding ARDS respondents. Should these differences result in a selection bias, its direction would increase the relative proportions of severe ARDS patients included in our sample, which would probably result in a worse HR-QOL.

Several long-lasting effects of ICU stay have been described after ARDS, including posttraumatic stress disorder [6], cognitive sequelae [8], and the rehabilitation phase after a long, debilitating hospitalization [11]. Therefore one can expect reductions in HR-QOL in ARDS survivors, related either directly to residual pulmonary dysfunction or to prolonged ICU stays. This study suggests that these reductions may not be distinguishable from those in other critical patients with similar age and matched for severity of disease and previous health state.

Two main conclusions may be driven from this study. Firstly, HR-QOL of ARDS survivors may not differ from HR-QOL of other ICU survivors, which should encourage early and aggressive treatment of ARDS to improve survival. Secondly, as with other authors [5, 6, 7], we were able to identify some of the sequelae of these survivors, so ARDS survivors should be included in follow-up clinics to reduce the long-term effect of the sequelae and to help them recover to their previous level of HR-QOL more quickly and more efficiently.

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