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Pulmonary Diffusion Capacity and Quality of Life during a Period of 6 Years in Patients who Survived Acute Respiratory Distress Syndrome

Lamot LE[1*], Quispe Laime AM[1,2], Fiore C[1,2], Martinez LR[1], Bettini JE[1], De Salvo AB[1], Fuks VE[1] and Petasny M[1]

[1]*Municipal Hospital of Agudos, Dr. Leonidas Lucero, Bahia Blanca, Buenos Aires, Argentina*

[2]*National University of the South, Bahia Blanca, Buenos Aires, Argentina*

[*]**Corresponding author:** Lamot LE, Hospital Municipal de Agudos, Dr. Leonidas Lucero, Bahia Blanca, Buenos Aires, Argentina; Tel: 54291154704296; E-mail: lauralamot@hotmail.com

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Abstract

Introduction: Patients who survived Acute Respiratory Distress Syndrome (ARDS) may present long term physical damage that affects their quality of life and respiratory capacity. Restrictive ventilatory disorders, decrease in pulmonary diffusing capacity and changes in quality of life were observed.

Objective: Know whether there are changes in pulmonary function and quality of life of patients who were discharged from the Intensive Care Unit (ICU) from 2008 to 2013, who required mechanical ventilation and presented ARDS.

Methods and Materials: Descriptive study: Observational study.

Inclusion criteria: Patients older than 18 years old, who required Mechanical ventilation, presented ARDS and have been discharged from the ICU for 12 months or more.

Exclusion criteria: Patients with severe ARDS caused by influenza or incapable of performing respiratory function studies. This study was conducted with institutional approval and informed consent. The following tests were carried out: Self-administered quality of life questionary (EQ–5D), spirometry, 6-minute walking test(6MWT), pulmonary diffusion test for CO (DLco), and lung volumes by nitrogen dilution performed with the computerized equipment Ultima™ Series Med Graphics.

Results: 13 patients were studied. The median age was 42 ± 15 years old, 76.9% male. Quality life perception shows through EQ-5D changes in the 5 components. The biggest change occurred in the pain/discomfort dimension with a median of 1.62 ± 0.506, and the EQ% health was 80.77% ± 12.05. The median values of the rates (FEV1, FVC, FEV1/FVC, FEF25/75) were over 80%. 5 patients presented a mild restrictive pattern.

Lung volumes and DLco showed median over 80%. 4 patients presented a mild alteration in diffusion and one of them presented desaturation during the 6MWT. Correlation between DLco% and EQ% health p=0.294, EQ% health-TTO p=0.001 and EQ% health-VAS p=0.001.

Conclusion: Our results suggest that patients with mechanical ventilation and severe ARDS who were evaluated after a year of being discharged from the ICU present mild pulmonary sequels and their quality of life was moderately affected. These results are similar to what is reported in the bibliography. A limitation to the study is the small size of the sample.

Keywords: Distress syndrome; Pulmonary function; Mechanical ventilation; Obesity

Introduction

Acute Respiratory Distress Syndrome (ARDS) is characterized by severe dyspnea and hypoxemia, which requires mechanical ventilation (MV) and hospitalization in the ICU. Even though this syndrome has been known from more than 50 years, it was not until 2011 that a definition by consensus was achieved (Berlin 2011), which allowed to classify the symptoms in mild, moderate and severe.

Despite the advances achieved in ventilatory management and therapeutical strategies, it is a disease commonly associated with a high mortality rate.

Traditionally, critical care evaluation was centred in mortality. However, in recent years, the objective of intensive medicine in critically ill patients is not only to ensure their survival, but also to achieve an ideal status of health. Since 2002, some studies have focused in functional consequences and quality of life of ARDS survivors. These studies have observed an alteration in their health related quality of life (QOL) and their pulmonary function [1].

The results show considerable alterations in the QOL in relation to the healthy reference sample subjects. They were put to test in different contexts and they showed a significant reduction in both generic health rates (Medical Outcome Survey 36-item short-form health survey (SF-36) and the EuroQol 5-D (EQ-5D) and in specific scales that evaluate pulmonary function. Most patients presented a mild restrictive pattern and a decrease of co-diffusion, as well as alterations in CT with reticular pattern and a moderate deficit in their exercising capacity in the Walking test.

In patients who survived ARDS a number of functional alterations are observed, which mostly disappear with the passage of time. Restrictive-type ventilatory disorders predominate in the early stages of recovery. Approximately one-third of patients have decreased total lung capacity, and nearly half of them have reduced pulmonary carbon monoxide transfer capacity (DLCO) [2]. The long-term quality of life depends mainly on the diagnostic category of ARDS, prolonged mechanical ventilation, severe trauma and severe sepsis are those that have strong reductions in the quality of life, mainly in the mental and emotional aspects. We decided to follow up and evaluated on the 13 survivors who were discharged ICU HMALL on 2009-2013. Evaluating lung function and quality of life for more than 12 months in order to know our experience.

Objective

To know whether there are alterations in pulmonary function and quality of life of patients who were discharged from the ICU between the years 2008-2013, required mechanical ventilation support, and presented ARDS.

Materials and Methods

Case series. Descriptive study. Observational.

Inclusion criteria: Patients older than 18 years old, who required MV, presented ARDS and have been discharged from the ICU for 12 months or more.

Exclusion criteria: Patients with severe ARDS caused by influenza or incapable of performing respiratory function studies. The study was conducted with institutional approval and informed consent. Patient selection was done through the ICU data base [3]. The intensive care unit is a multipurpose unit with a capacity of 14 beds, each equipped with different levels of complexity in a hospital of third level of care [4,5].

All patients included received treatment based on hospital protocols, which includes the protocol for ARDS following recommendations of the American Thoracic Society (ATS). Demographics and medical data were collected as part of routine clinical care: Acute physiologic and Chronic Health evaluation (APACHE II), scores of multiple organ failure (SOFA), laboratory values, ventilator data, neuromuscular lock and outcome data. All patients were contacted by telephone and there was an appointment with an informative interview to explain to them the objectives, implications and significance of the study. They were then invited to participate with their informed consent [6].

They took the self-administered quality of life questionnaire (EQ-5D), the 6-minute walking test, spirometry, the pulmonary diffusing capacity for CO(DLco), and lung volumes by nitrogen dilution performed with the computerized equipment Ultima™ Series Med Graphics according to ATS standards. We used the Spanish validated EQ-5D version, which is a generic and simple instrument composed of three parts: A descriptive system which describes a health status in 5 dimensions, a visual analogue scale (VAS), and a demographic categorization.

The descriptive system comprises 5 dimensions: Mobility, personal care, everyday activities, pain/discomfort, and anxiety/depression. Each dimension is divided in three levels: Level 1=no problems; level 2=some/moderate problems; and level 3=many problems. The VAS is 20 cm long with scores from 0 to 100, where 0 and 100 represent the worst and the best imaginable health status respectively, expressed as EQ% health [7,8].

Demographic categorization consists of obtaining individual values. The reference values taken are the ones developed by Argentinians. Based on EQ-5D and using the visual analogue scale (VAS) and time-trade-off (TTO) with models of logistic regression, they proposed a VAS rate 0.858 and TTO rate 0.908. The DLco study was conducted through the single breath method with determination of blood capillary pulmonary supply and membrane diffusing factor. From its components, the alveolar volume and the permeability coefficient were interpreted [9].

Statistical analysis

Statistical analysis was done with SSPS 19.0.

Discrete variables were registered as percentages and continuous variables as averages plus/minus a standard deviation, medium, and minimal-maximal values. Non parametrical tests and general lineal model were carried out [10-12].

For the patient's clinical and functional characteristics, group differences were evaluated using statistical Chi2 and Z of Kolmogorov-Smirnov. Correlation between variables was done with Spearman and Pearson's Rho coefficient. A p value equal or minor to 0.05 was considered as significant.

Results

The total number of patients admitted to the ICU for severe ARDS from 2008 to 2013 was 70, 25 of whom had died, 13 patients were studied, and 32 patients were excluded (12 for ARDS caused by influenza, 3 for being unable to carry out the studies, 4 patients did not want to participate, and we could not contact the other 13 patients).

Their mean age was 42 ± 15 years old and they were males: 76.9%. The mean stay in the ICU and in hospital was 17 ± 35 and 29 ± 54 respectively. The mean of days in MV was 14.54 ± 5. The mean APACHEII and SOFA Day 1 was 13, 69 ± 6,061 and 5, 31 ± 2,626 respectively. The relevant antecedents were smoking in 69.2% (8/13) and obesity-overweight in 68.5% (9/13). The mean BMI of the patients was 30.79 ± 9.52 (Table 1).

Age, smoking, cause of ARDS or baseline disease were analyzed with contingency tables, T-tests and correlation, and had no impact on the results found in quality of life or pulmonary function. In the 13 patients evaluated by EQ-5D after more than a year of being discharged from the ICU, perception of their quality of life shows changes in the 5 components. The pain/discomfort dimension is the one with more change with an average of 1.62 ± 0.506, and the personal care dimension is the one with less change with an average of 1.15 ± 0.55 [13]. The result for the health status through the VAS

expressed as EQ% health showed an average of 80.77% ± 12.05, with a scope of 70-100%.

The valuation for demographic categorization in relation to the validated data for Argentina was for TTO and average of 0.81 ± 0.216 and for VAS and average of 0.78 ± 0.249 (Table 2).

Variable	Age	Days UCI	Days MVA	Days hospital	Height cm	Weight kg	BMI
Mean	42.23	26.46	14.54	52.15	172.38	92.85	30.792
Median	40	17	13	29	175	84	27.4
DS	15.227	35.669	5.109	54.682	9.014	31.323	9.5213
Minimum	23	13	9	18	147	55	20
Maximum	67	143	23	179	183	147	47.9
IC 95%	33-51	11.4-17.6	4.9-4.8	19.1-85.2	129.8-188.7	63.1-111.8	21.6-36.8
ICU: Intensive Care Unit; MVA: Mechanical Ventilatory Assistance; BMI: Body Mass Index							

Table 1: General characteristics.

Variable	EQMO	EQCP	EQATD	EQD/M	EQA/D	EQ% health[a]	TTO[b]	VAS[b]
Mean	1.46	1.15	1.31	1.62	1.31	80.77	0.81	0.78
Median	1	1	1	2	1	80	0.89	0.85
DS	0.519	0.555	0.630	0.506	0.630	12.050	0.216	0.249
Minimum	1	1	1	1	1	70	0.21	0.63
Maximum	2	3	3	2	3	100	1	1
IC 95%	1.15-1.78	0.82-1.46	0.93-1.69	1.31-1.92	0.93-1.69	73.49-88.05	0.68-0.98	0.63-0.93
Q-5D Dimensions: EQ MO=Motility; EQ CP=Personal Care; EQ ATD=Everyday Activity; EQ D/M=Pain/Discomfort; EQ A/D=Anxiety/Depression [a]EQ% health: State of health on a visual analog scale from 0 to 100% [b]Preciation or indices. According to validation for Argentina: TTO=Time-trade Off; VAS=Visual Analog Scale.								

Table 2: Perceived quality of life EQ-5D.

Basal spirometry and post-bronchodilator showed an alteration of pulmonary function in 5 patients. They all presented mild restrictive component and 3 a mixed pattern. The median values of the rates (FEV1, FVC, FEV1/FVC, FEF25/75) were above 80% (Table 3).

Variable	PB%Pron	PtB%Pron	PBP%Pron	PtB%Pron	PB%Pron	PtB%Pron	PB%Pron	PtB%Pron
	FVC	FVC	FEV1	FEV1	FEV1/FVC	FEV1/FVC	FEF25-75	FEF25-75
Mean	83.42	80.75	82.33	84	78.67	102.50	72.64	97.75
Median	87	79	86	80	80	104	79	93
DS	14.100	13.451	19.611	16.733	3.085	5.196	31.522	17.056
Minimum	59	67	48	70	73	95	70	84
Maximum	98	98	104	106	83	107	115	121
IC 95%	74.46-92.38	59.35-102.15	69.87-94.79	57.37-110.63	76.71-80.63	94.23-110.77	30.9-115	70.61-124.8
PB % Pron (pre-bronchodilators): FVC. FEV1. FEF 25-75 PtB % Pron (post-bronchodilators): FVC. FEV1. FEF 25-75								

Table 3: Spirometry.

Lung volumes and DLco showed average values above 80%. 4 patients presented a mild alteration of diffusion (Table 4).

Variable	%SCV[a]	%FRC[a]	%TLC[a]	%RVTLC[a]	%DLCOcor[b]	%DLVA[b]	%VA[b]
Mean	85.36	85.08	85.17	84.75	89.33	111.42	83.17
Median	90	83.50	82	85	88.50	111.50	82
DS	12.933	23.173	15.008	25.252	15.305	15.389	11.885
Minimum	63	53	59	47	68	88	64
Maximum	101	130	114	135	108	138	108
IC 95%	76.68-94.05	70.36-99.81	75.63-94.7	68.71-100.7	79.61-99.06	101.6-121.19	75.62-90.72

[a]Pulmonary volumes (L): SVC (vital capacity); FRC (functional residual capacity); TLC (total lung capacity); RV/TLC (residual volume adjusted to total lung capacity).

[b]Diffusion (mL/min/mmHg): DLCO (pulmonary diffusion for carbon monoxide); DL/VA (alveolar volume-adjusted lung diffusion); VA (alveolar volume).

Table 4: Pulmonary volumes and diffusion CO (DLco).

The 6-minute walking test showed that 6 patients could go through a shorter distance than expected. Being obesity/overweight a relevant antecedent. Desaturation was observed in 2 patients with a minimum register of 81%. However this was correlated with alterations in other functional studies. One of the patients presented HIV+ as a relevant antecedent and hospitalization for pneumonia caused by *pneumocystis jirovecci* [14]. No relation was found between the variables of pulmonary diffusing capacity valued in % DLco (0 to 110%) and the perception of quality of life valuated by EQ% health (0 to 100%). Pearson 0.331 (bilateral significance 0.294) and Spearman's Rho Coefficient 0.181 (bilateral significance 0.287). Contrastive analysis (X^2): DLCO p=1.0; EQ% Health p=0.99; TTO p=0.48; VAS p=0.556 (Figure 1).

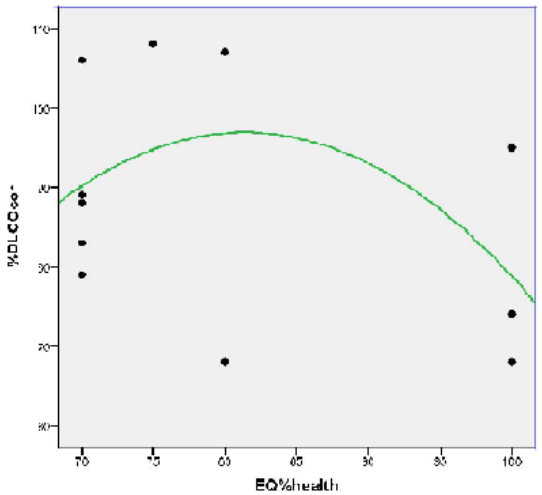

Figure 1: Correlation between pulmonary diffusion and quality of life. Pearson 0.331 (p=0.294) and Spearman's Rho 0.181 (p=0.287).

Health perception EQ% health was correlated with rates TTO and VAS in pairs. EQ% health-TTO and EQ% health-VAS. A good correlation between these variables was observed. Pearson: For EQ% health-TTO 0.678 (bilateral significance 0.004) and for EQ% health-VAS 0.734 (significance 0.001). Spearman's Rho Coefficient: For EQ% health-TTO 0.811 (significance 0.001) and for EQ% health-VAS 0.850 (significance 0.001) (Figure 2).

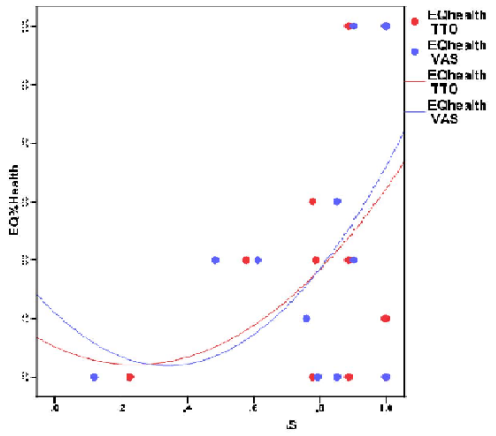

Figure 2: Correlation between EQ% health with TTO and VAS

Discussion

Although our patient sample is small, results suggest that after more than a year of being discharged from the ICU. Patients present alterations in their quality of life and pulmonary function.

Patients with influenza-elicited ARDS have different functional behaviour than other etiologies. During the viral replicative phase the deregulated inflammatory response occurs in a self-limited manner with minor sequelae after the acute phase. In our limited experience we have analyzed the pulmonary sequelae and the quality of life during the 2009 pandemic. Observing that they did not present deterioration

of lung function unlike other etiologies which is why we have excluded these patients [15-17].

Regarding quality of life we observed that there is a moderate deterioration in all the dimensions evaluated by the EQ-5D, the greatest change observed in the pain-discomfort dimension. The analysis of quality of life using Argentinian reference shows a decrease for the whole series.

Other authors have proven a reduction in different scales with greater limitations in physical ability, anxiety/depression and a decrease in the perception of health of 30%.

The pulmonary function studies show a mild degree alteration in spirometrical parameters, volumes and DLCO with a predominantly restrictive pattern [18].

The motion test evaluated submaximal exercise in patients, which, in spite of not valuating maximum effort, is useful in the monitoring and detection of limitations in everyday activities. Patients who presented a decrease in DLCO also presented an alteration in the motion test with perception of dyspnea and/or desaturation.

Other author's studies have evaluated pulmonary function for a period of 6 years after ARDS and have similar results to our sample with vital capacity, restrictive pattern and decrease in DLCO with alterations in CT in 76% of the patients [19].

We found that there was no correlation between respiratory functional behaviour and well-being, and that the valuation for TTO and VAS rates showed correlation to EQ% health. A limitation of our work is a small case series and a retrospective study however, it is interesting to know the impact of respiratory function in order to develop better therapeutic strategies

Conclusion

In our population the results suggest that the survivors of ARDS have mild pulmonary sequelae and a moderate impact on their quality of life. These results are similar to what is reported in the bibliography. A limitation to the study is the small size of the sample, however these findings allow us to create hypotheses for prospective studies and to develop strategies to prevent or improve the quality of life and the sequelae of our patients.

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