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Respiratory Profile in Patients After Liver Transplantation

M.M.C. da Silva*, R.A. Corcha, A.M. Oliveira da Silva, F.J.B.Z. Franco, J.R. de Souza Almeida, and I.F.S.F. Boin

Gastrocenter Unicamp, University City, Campinas/SP, Brazil

ABSTRACT

Background. Patients in the immediate post-operative liver transplantation (LxT) period can develop respiratory and functional complications. In the postoperative months, these functions tend to improve. Nevertheless, there are few studies that evaluate precisely and specifically respiratory function in post-LxT long-term after surgery. The objective of the study was to describe the respiratory profile of patients 1 to 6 months after LxT, accompanied by LxT outpatients.

Methods. We included patients between 25 and 60 years old. We excluded patients with chronic renal or cerebrovascular impairment, severe heart disease, and history of lung surgery or liver re-transplantation. Evaluations were carried out on 3 occasions: 1 month, 3 months, and 6 months after LxT. The following evaluations were submitted: respiratory muscle strength (manuvacuometer), value flows and lung volumes (spirometer), and surface electromyography analyzing root mean square in the right (RMS-R) and left (RMS-L) diaphragm. We analyzed MELD (Model for End-Stage Liver Disease). After normality tests, we used the Friedman test (non-parametric values) and ANOVA (parametric values), $P \geq .5$ with the use of SPSS 21.0.

Results. Patients (n = 15) had a mean age of 53.0 ± 7.5 years and 25.9 ± 4.6 MELD score. The statistically significant value obtained at the 3 occasions of evaluation was RMS-R, with a decline during periods of evaluation. This can be caused by removal of the liver, resulting in a denervation and reduction in compliance of this portion of the muscle.

Conclusions. Patients between 1 and 6 months after transplantation have a specific respiratory profile, close to normal values. However, there are few studies on this subject, and we suggest that more research be done.

LIVER transplantation (LtX) is the only effective treatment for acute liver failure in advanced stages [1]. In addition to the metabolic changes arising from the organ failure, patients face long wait-list times [2]. Thereby, such patients may present breathing modifications such as atelectasis, pleural effusion, and low pulmonary complacency, thus affecting the alveolar functioning and the gas exchange before the surgery stage [1].

Soon after surgery, new functional and respiratory complications usually emerge. Huang et al [1] unveiled in their study that liver transplantation is an upper-abdominal surgery, in which abdominal muscle lesions occur (rectus and oblique) and are often associated with lung movement (respiratory mechanics).

Another study corroborating this information states that "the anesthesia, surgery trauma, and the post-op attached conditions (incision, drainage, and catheter) have an impact on respiratory mechanics and on patient mobility" [3].

All these factors, associated with pain, coughing difficulty, and immobility, lead to post-operative pulmonary complications.

*Address correspondence to Marcela Maria Carvalho da Silva, Av. Engenheiro Augusto Figueiredo, No. 357, Apartment 105, Tower 6, Campinas/SP, Brazil. E-mail: marcelacarvalhofisioterapia@yahoo.com.br

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A study on upper-abdominal surgery patients in which preoperative and post-operative data were assessed (first, seventh, and 30th days after surgery) showed that all patients presented a decrease in respiratory muscular performance as well in spirometric parameters soon after surgery. However, on the 30th day, they tended to return to their proper functioning, which have been diminished before the surgery [3].

Barcelos et al [4] also evaluated the pulmonary capacity through spiromometry and manuvacuometry for 30 patients equally allocated into 6 groups: liver transplantation and 1, 3, 6, 9, and 12 months after the transplantation. Patients had some increase in pulmonary capacity despite not being statistically meaningful.

Throughout the months after surgery, patients tended to have improvement in functions. Vital forced capacity (VFC) and FEV1 (forced expiratory volume on the first second) from these groups had no significant variations, demonstrating some tendency to progressive improvement for pulmonary capacity after transplantation. On the same grounds, there was some improvement in maximum inspiratory pressure after surgery.

Respiratory function is greatly decreased in the early stages for the liver after transplantation, and there is a scarcity of long-term studies for this function. It is fundamentally important to create a respiratory profile for an extensive period for these patients so that we can comprehend the main alterations that may result and develop intervention for exactly when these situations occur.

METHODS

Inclusion criteria for this prospective study included patients between 25 and 60 years old, submitted 1 month after LxT. Patients were followed up by the physiotherapy team of Gastrocenter Unicamp, after signed informed consent was obtained. All patients who had a history of pulmonary surgery or liver re-transplantation were excluded, as well as those with chronic renal impairment, established sequel of global motor function or cognitive cerebrovascular disease, and grave heart conditions such as unstable angina or vascular obstruction. The inability to carry out the proposed tests was an eliminatory factor.

After the volunteer selection analysis, according to its established inclusion and exclusion criteria, the patients were invited to a 1-month post–liver transplantation conversation at the gastrocenter outpatient facility.

Three assessment stages were defined: I) 1-month after liver transplantation; II) 3 months after liver transplantation; and III) 6 months after liver transplantation.

Assessments consisted of an evaluation of respiratory muscle strength, pulmonary function proof, and underlying muscle tissue bilateral diaphragm electromyography. These were performed throughout the whole researching protocol.

To evaluate flow and lung volumes, spirometry was measured with the use of EasyOne Diagnostic Spirometer Word (Zurich, Switzerland); we analyzed forced vital capacity (FVC); forced expiratory flow 25% to 75% (FEF 25%–75%); and forced expiratory volume in the first second (VEF1).

To measure electrical activity of the diaphragm muscle bilateral surface, electromyography (sEMG; EMG System of Brazil Ltd, series 00405, model 210C; San Paulo, Brazil) was used. While the subjects rested at 45°, one electrode was placed on the xiphoid process; another was placed 15 cm from the xiphoid process at the right diaphragm and the third 15 cm from the xiphoid process at the left diaphragm, with the lower ribcage margin used as reference. The fourth was placed on the left hand to avoid interference. The collected data of root-mean-square (RMS) right (R) and left (L) were analyzed and recorded with the use of the notebook (Intelbras I21, San Paulo, Brazil). Respiratory muscle strength was measured with the use of a manometer [maximal inspiratory pressure (MIP) and maximal expiratory pressure (MEP) in cm H_2O] through manovacuometry (−300/+300, Ger-Air San Paulo, Brazil), with subjects in the seated position; the best result of three was recorded.

Other data collected were Model for End-Stage Liver Disease (MELD) [5] scores and vital signs.

For descriptive statistics, the SPSS 21.0 (2012) program (Armonk, NY, United States) was used ($P < .05$). Kolmogorov-Smirnov and Shapiro-Wilk normality tests for each variable were used. For symmetric values, mean values were used; the asymmetric the median 1 was applied.

The Friedman statistical test was used for non-parametric values and analysis of variance test (ANOVA) for parametric data. To compare proportions, we used the Chi-square test.

The study was approved by the Ethics Committee of The Faculty of Medical Sciences, State University of Campinas, −San Paulo, Brazil; No. 922/2009.

RESULTS

We included 15 patients in this research, which has never been done before with such a specific sample of people. Two patients died and 5 patients had clinical complications or abandoned the study before completing 6 months after LxT. In total, 38% were women and 62% were men. The average age was 53.0 ± 7.5 years, and the average MELD without additional points was 25.9 ± 4.6.

The measurements of profile respiratory evaluations are shown in Table 1. Values were measured in 3 stages; they were 1, 3, and 6 months after the transplantation and were separately compared on an evaluative manner up to drawing a respiratory profile for those patients in the course of 6 months after the transplantation.

Table 1. Median or Median of Variables at Three Evaluations, According to Respiratory Muscle Strength, Flow and Lung Volumes, and Surface Electromyography

	1 Month	3 Months	6 Months
RME			
MIP (cm H_2O)†	82.5	85.0	100.0
MEP (cm H_2O)†	90.0	90.0	90.0
FVCl	72.67 ± 17.86	76.25 ± 16.27	83.43 ± 11.14
FLV			
FEF 25%–75%† (L/min)	83.5	78.5	92.0
VEF1 (L)	75.75 ± 15.92	78.38 ± 16.41	86.43 ± 10.50
RMSR (μV)*,†	34.9	31.64	37.0
sEMG			
RMSL (μV)†	33.3	30.55	35.3

Abbreviations: RMS, Respiratory muscle strength; FLV, flow and lung volumes.
*$P < .05$.
†Values of asymmetric median were applied.

Table 2. Demographic and Clinical Features

Pre-operative	
Age (years)	53.0 ± 7.5
Sex (%)	
Female	38%
Male	62%
Previous smoker (%)	50%
BMI (kg/m^2)	24.34 ± 3.49
DH (days)*	4.89
WT (months)*	7.0
MELD	25.9 ± 4.6
Child (%)	
A	28.6%
B	42.8%
C	28.6%
Ascites (%)	
Light	87.5%
Moderate	12.5%
EH (%)	
Absent	20%
Grade 1	20%
Grade 2	60%
Original disease (%)	
AC + HCC	12.5%
AC	37.5%
HCC	37.5%
HT + HCC	12.5%
Donor source	
Age (years)	45.5 ± 19.2
Sex (%)	
Female	38%
Male	62%
Localization	Max 250 km distance
Cause (%)	
CVA	62%
TBI	38%
Surgery	
Type of operation (%)	100% Orthotopic liver transplantation
Technique of operation (%)	100% Piggy-back

After Liver Transplantation: Laboratory exams/LFT	1 Month	3 Months	6 Months	Reference Value
AST (U/L)*	28	22.5	22	10–30
ALT (U/L)*	27	21.5	20.5	10–40
GGT*	79.5	32	53.5	10–60
Bilirubin (mg/dL)*	0.7	0.6	0.92	0.2–1.0
Albumin (g/dL)	4.25 ± 0.45	4.61 ± 0.21	4.57 ± 0.33	3.4–4.8
Creatinine (mg/dL)	1.18 ± 0.44	1.04 ± 0.32	1.06 ± 0.27	0.4–1.2
INR*	1.13	0.22	1.11	<1.25
Platelets (mm^3)	192.250 ± 121.000	127.5	137	150.000 ± 400.000

Abbreviations: BMI, body mass index; DH, duration of hospitalization; WT, alcoholic cirrhosis; MELD, Model for End-Stage Liver Disease; Child, classification of Child-Turcotte-Pugh; EH, hepatic encephalopathy; AC, alcoholic cirrhosis; HCC, hepatitis C virus cirrhosis; HT, hepatic tumor; CVA, cerebrovascular accident; TBI, traumatic brain injury; LFT, liver function test; AST, aspartate aminotransferase; ALT, alanine aminotransferase; GGT, gamma-glutamyl transpeptidase; INR, international normalized ratio.

*Values of asymmetric median were applied.

Table 2 provides the demographic and clinical characteristics of patients included in the statistical analysis. No patient studied had severe infection or acute rejection episodes during the 3 evaluations.

Complications related to health were observed: 2 patients presented abdominal pain during the 3-month evaluation; abdominal hernia and "started smoking again" also occurred.

DISCUSSION

The mean age was in accordance with national [4,6] and international studies [7] in post-LxT patients.

The average value of MELD scores was higher compared with another study [5] carried out at the same research center showing the patients' poor clinical state.

In the present study, we note that the measurement obtained at the first evaluation, which showed the average of MIP, is in accordance with the expected normality for the average of the studied population. In agreement with these data, a study with patients after cholecystectomy, which evaluated their respiratory muscle strength, concluded that after 10 days of surgery, the MIP returns to the initial value of normality [2].

Concerning MEP, a study concluded that there was no statistical difference between pre- and post-transplantation groups (1, 3, 6, 9, and 12 months) [4]. Thus, its data are in accordance with our results, which showed MEP remaining the same at the 3 evaluations.

The results for the 3 evaluations of pulmonary function tests showed no statistical difference, and thus the values were considered normal for this population.

According to Barcelos et al [4], pathophysiological changes in post-operative liver transplantation are observed: volumes and vital capacity are reduced in because of the large surgery incision and diaphragmatic dysfunction. After 7 to 10 days, this function returns to values considered normal for the population studied.

Therefore, the values obtained in the pulmonary function test in FVC and FEV1 resulted in no statistical difference among the evaluations. This also occurred in another study [4]. For this reason, we suggest a new study involving a larger number of patients to obtain a more reliable statistical result.

FEF 25%–75% values at the second evaluation were decreased values, but without statistical difference, which could be justified by the presented abdominal pain in this stage.

We found no studies that discuss the use of sEMG applied after upper-abdominal surgery or liver transplantation. However, some findings were from right diaphragm electroneuromyography, carried out on liver transplantation waiting list candidates and developed at the same research center [8].

This study showed the values of the average RMS (R) for the healthy population, which were 49.1 ± 17.6, whereas patients' waiting-list LxT had a value of 61.0 ± 68.5. We therefore concluded that the RMS (R) on patients after 1 month of transplantation showed a higher value than that considered normal (healthy population) [8–10] RMS (R) had a statistically significant decline in the values comparing 3 evaluation periods. This can be due to a diaphragmatic lesion, which occurs after surgical manipulation for liver removal, causing a denervation and reduction on compliance of this portion of the muscle.

The RMS (L) showed no statistically significant difference among the 3 periods. Two hypotheses are possible and deserve further studies. First, the liver is anatomically located in the right portion of the diaphragm, whereas the left manipulation is minimal, generating a minimal diaphragmatic change on this side. Another possibility is that the number of patients studied is limited.

Comparing the values obtained with the pulmonary function test and respiratory muscle strength, we verified that they reached values close to statistical significance.

Patients between 1 to 6 months after transplantation have a specific respiratory profile, close to normal values. However, there are few studies on this subject, and we suggest that more research be done.

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