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Success or failure predictive indexes of extubation in renal transplants patients under mechanical ventilation – pilot study

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ABSTRACT

Introduction: Currently, chronic kidney disease (CKD) is a major health problem and in the most severe conditions, kidney transplantation is an alternative treatment. However immunosuppression induced these patients to respiratory complications and endotracheal intubation. In order to assist the decision of the best time for weaning and extubation of these patients, there are predictive indexes that should be considered in preliminary assesment. **Objective:** To check the capacity of predictive indexes for weaning of mechanical ventilation, rapid shallow breathing index (RSBI), oxygenation rate (PaO_2/FiO_2) and maximum inspiratory pressure (MIP) in predicting the success or extubation failure in kidney transplant patients. **Methods:** This study is a prospective cohort carried out with patients aged over 18, under mechanical ventilation for more than 24 hours. The patients were submitted to the Spontaneous Breathing Test, also the assessment of the Rapid Shallow Breathing Index, oxygenation index (PaO_2/FiO_2), and maximum inspiratory pressure (MIP) and they were observed during 48 hours after to evaluate the success and extubation failure. **Results:** A total of 106 patients were eligible, and 20 of these were included with mean age of 46.9 ± 3.06 years and 14 of the subjects were male. Three patients showed extubation failure, and needed to have reintubation within the period of 48 hours as considered. **Conclusion:** The indices to predict weaning of mechanical ventilation, when within the expected normal values, seem to be able to predict extubation, with the exception of MIP that, even in cases of success, showed itself to be at levels lower than the predicted percentage.

Keywords: mechanical ventilation, ventilator weaning, chronic kidney failure, kidney transplantation, breath tests

INTRODUCTION

Chronic kidney disease (CKD) is today an important public health problem and in Brazil the number of individuals on dialysis programs more than doubled in the last eight years. [1] It is an irreversible condition which can be potentially fatal, in addition, chronic renal patients can develop several comorbidities associated with the disease and dysfunction in multiple systems, such as bone, muscle, cardiovascular, metabolic and respiratory, and the lung can be one of the most affected organs. [2]

Kidney function and lung function working closely related and when kidney function goes into bankruptcy, we can understand that the lung will be directly affected, this is not only due to changes in acid-base balance, but also by the fact that the kidney have to balance the blood volume. [3,4]

In view of all the problems and complications that individuals with CKD are exposed, the kidney transplant comes as an outlet for the increased survival rate and the decrease of comorbidities associated with the disease, with best cost-benefit ratio in the case of patients in advanced stage. [5-7]

All kinds of solid organ transplants predispose infections and pneumonia is the most common infection. This occurs because the individuals need to receive anti-rejection drugs (immunosuppressive) that increase the success of the transplant and the chances of developing this type of infection, associating to extended hospitalizations, need to use orotracheal intubation and inability of airway protection. [4]

Respiratory diseases associated with immune suppression condition tend to complicate the condition of these patients and often the necessity of the use of mechanical ventilation is inevitable. According to Canet, [5] 47,8% of ICU individuals are admitted with a diagnosis of respiratory failure and require ventilatory support. The use of positive pressure ventilation

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may cause renal hypoperfusion which decreases even more functionality and for these patients is extremely critical considering that they already have naturally reduced renal function due to pathophysiology of the disease itself.

Faced with the gravity of these patients, it is necessary to pay special attention in order to find the best time for weaning and extubation of mechanical ventilation. The weaning index has been a tool used by intensive care specialist to ensure the best time to discontinue the ventilatory support and the accuracy of these instruments makes the process safer for the patient and the team. [2, 4-6]

But clinical practice should be considered, so when starting the weaning phase some criteria need to be well defined. The main ones are: whether the causes which led to respiratory failure and mechanical ventilation were resolved, what are the guidelines used to reduce ventilatory support and the criteria for extubation.[7,8] According to Mancintyre, 42% of mechanical ventilation time is for the process of weaning from ventilation, [8] but the extubation success will also depend on the degree of immunosuppression, nutritional status, metabolic balance and stabilization of associated comorbidities. [9]

Even after the success of the transplant, the presence of frequent infections, the need for mechanical ventilation and immobility lead these patients to sequels, such as significant loss of muscle fibers and irreversible lung problems that associated with chronic kidney condition, can hamper the weaning and extubation of patients.[10, 11]

In view of the above, the justification of this study was to evaluate which of the weaning index of mechanical ventilation would be more reliable during the process of weaning and extubation of kidney transplant patients, aiming at the implementation of protocols in these units, since these patients require intense vigilance due to the condition of immunosuppression.

The aim of this study was to verify the ability of predictive weaning indexes from mechanical ventilation, rapid shallow breathing index (RSBI), oxygenation index ($PaO_2/FiO_{2)}$ and maximum inspiratory pressure (MIP) in predicting the success or failure on extubation in the population of chronic renal transplant individuals and assess which of these indexes measured have a higher effectiveness in predicting success/failed extubation.

METHOD

Study design

Prospective cohort study conducted in the intensive care unit (ICU) of the Hospital of kidney and Hypertension of Universidade Federal de São Paulo (UNIFESP), from September 2014 to March 2015, in accordance with ethical standards of UNIFESP (CAAE: 02036012.2.0000.5505). The consent form was distributed and signed by the person responsible for all patients.

Sample Characterization

20 patients under mechanical ventilation with orotracheal intubation were analyzed, these being immediate or late renal transplant recipients, according to the following inclusion criteria:

- More than 18 years old.
- Mechanical ventilation time greater than 24 hours, as III Brazilian Consensus of mechanical ventilation. [12]
- Clinical improvement (reversal of the cause that led to mechanical ventilation).
- Adequate oxygenation (PaO_2 higher than 80 with 40% of FiO2 and with Peep lower or equal of 5-7 cmH_2O.
- Hemodynamic stability. Heart rate lower than 140 beats per minute. Without use of vasoactive drugs or use minimum doses.
- Respiratory rate lower than 35 rpm.
- Without sedation.

The tracheostomized individuals, patients in non-invasive ventilation and chronic kidney disease patients not transplanted were excluded.

Procedures

Previously to the realization of spontaneous breathing trial (SBT) were measured and collected the RSBI, PaO_2/FiO_2 and MIP, and VM used because they providing an overview of the strength capacity, endurance and gas exchange ability of individuals, in addition to being widely published in the literature. [9] Also, were collected other parameters such as: heart rate (HR), blood pressure (BP), oxygen saturation ($SpO_{2),}$ arterial blood gas and water balance. The choice of which type of SBT this individual would be submitted is made by intensivist team. In PSV ventilation mode or test tube - T, both choices are equally effective and safe to the patient. [12, 13] At the end, were collected the realization time of the patient, success or failure information during the procedure, reintubation within 48 hours and its causes. It was also evaluated the need for non-invasive ventilation post extubation, use of vasoactive drugs, if the patient was on hemodialysis or peritoneal dialysis and the SAPS (Simplified Acute Physiology Score) severity scores, which the higher is the score the worst is considered the patient's health status [14] and SOFA (Sepsis-related Organ Failure Assesment). [15]

For the measurement of MIP was using a manovacuometer (Instrumentation Industries^{R} – Pensilvania – EUA), without the aid of one-way valve, starting the cycle from the residual volume and keeping the occlusion as long as possible be tolerated by the patient through verbal encouragement and with the aid of nasal clip, considering the best result of three

consecutive collections. To obtain the predicted MIP was used the equation of Neder et al. [16]

To obtain the RSBI (f/VC) was measured the respiratory frequency (f) through a mouthpiece for one minute in which the patient was instructed to keep habitual breathing, was used a ventilometer (Ferraris^{R} – Colorado, EUA), to obtaining the tidal volume (VC) in liters [17] and for the analysis of PaO_2/FiO_2 was considered the arterial blood gas analysis and the value of the fraction of inspired oxygen (FiO_2) which the patient was being ventilated.

To the RSBI was considered the value of 60-105 [16] and to PaO_2/FiO_2 lower than 150 [8] as parameters of normality.

SBT was conducted over a period of 30 to 60 minutes, with the following parameters: pressure support ventilation (PSV) from 6 to 8 cmH_2O, positive end-expiratory pressure (PEEP) from 5 to 7 cmH_2O and FiO_2 up to 40%, or using T-tube with the support when necessary to maintain SpO_2.

Before being extubated, the patients were rigorously assessed according to the level of consciousness, degree of collaboration and the ability to cough to eliminate secretion of the lungs and/or upper airways.

In cases of SBT failure, the patient was forwarded to mechanical ventilation for 24 more hours to rest and may go through new SBT later.

It was considered as SBT failure: [8]

- Respiratory rate lower than 35 ipm.
- Arterial oxygen saturation lower than 90%.
- Heart rate higher than 140 bpm.
- Systolic blood pressure higher than 180 mmHg or lower than 90 mmHg.
- Signs and symptoms: shaking, sweating, altered level of consciousness.

The extubation failure was considered when there was need for reintubation during the first 48 hours. Individuals who presented extubation failure not passed again in the Protocol. [7]

In Figure 1 presents a simplified flowchart with the design of the study.

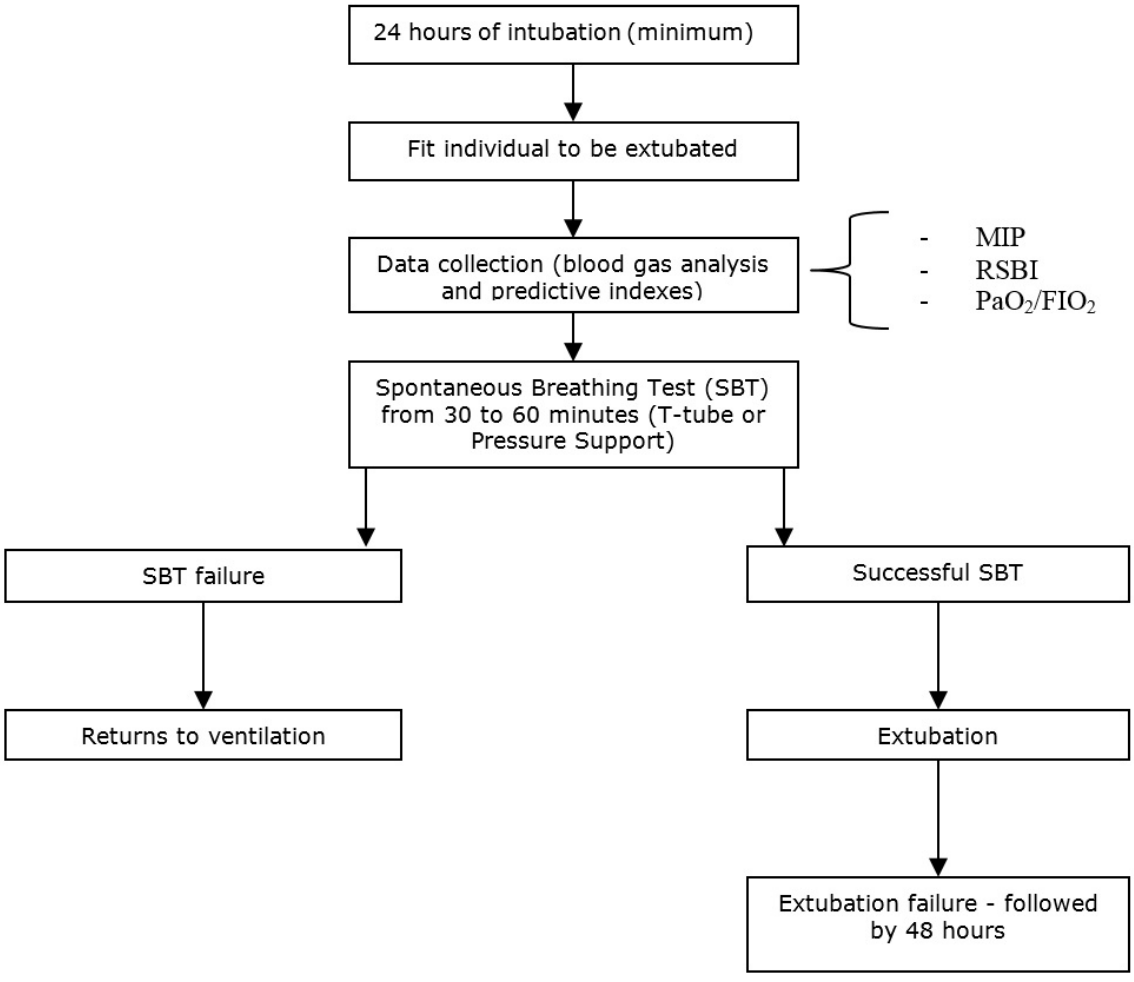

Figure 1. Flowchart of the study design. Subtitle: MIP = maximum inspiratory pressure; RSBI = rapid shallow breathing index; PaO2/FIO2 = oxygenation rate.

Statistical analysis

The number of patients involved in the study was based on a convenience sampling. All individuals on mechanical ventilation with orotracheal intubation were eligible. The numeric variables are presented in mean values and standard deviation and the categorical (hemodialysis) in frequency and proportion. There was not enough casuistry for comparison of means.

RESULTS

36 patients were eligible and 16 were excluded: 8 deaths, 2 tracheostomy, 2 extubations with less than 24 hours, 1 child, 1 accidental extubation, and 2 follow losses. Therefore, were evaluated 20 patients.

The age of patients ranged from 30 to 71 years, with an average of 46.9 ± 3.06 years, 14 male. The causes of intubation were diverse, being divided into: respiratory, surgical, cardiology, neurological and clinical.

Of the 20 evaluable patients, three (15%) patients developed extubation failure requiring orotracheal reintubation within the first 48 hours, these are presented, as Table 1, with greater age, higher BMI and higher blood pressure when compared to the successful group. The causes related to reintubation were: post-extubation respiratory failure, lowered level of consciousness and cardiopulmonary arrest.

In relation to weaning predictive indexes can be seen that PaO_2/FiO_2 and RSBI were within the expected values of normality in both groups, while MIP presented decreased in both groups (Table 2).

The three individuals of the failure group were submitted to SBT with PSV, and presented more tachypneic with worse oxygenation index, they also had to undergo to NIV post extubation.

In table 3 are described the clinical data and the severity index of these patients, in which can be observed that the weaning failed group showed metabolic acidosis, a more positive water balance, and the need for vasoactive drugs, when compared to the successful group. In relation to the gravity index, were collected SOFA [17] and SAPS [16] indexes, in which the percentage of predicted mortality was shown to be greater for the weaning failed group.

Table 1. Demographics, hemodynamics and arterial oxygen saturation of 20 patients evaluated.

Variables	Successful N=17	Failure N=3
	Mean (SD)	Mean (SD)
Male (N)	12	2
Age (years)	43.17 (11.14)	68 (2.64)
BMI (kg/m²)	25.7 (5.1)	31 (3.7)
HR (bpm)	91.35 (13.87)	70 (19.15)
SBP (mmHg)	130.82 (19.68)	155.33 (13.50)
DPB (mmHg)	70.94 (10.38)	85.66 (20.98)
SpO_2 (%)	96.11 (1.61)	95.33 (2.30)

BMI-body mass index; HR-heart rate; SBP – systolic blood pressure; DBP-diastolic blood pressure; SpO_2 - oxygen saturation.

Table 2. Data referring to the days of intubation, spontaneous breathing test and its parameters, weaning predictive indexes and use of noninvasive ventilation.

Variables	Successful N=17	Failure N=3
	Mean (SD)	Mean (SD)
TOT (days)	6.76 (5.86)	4 (3.46)
SBT (PSV/T-tube) (N)	15 / 2	3 / 0
SBT Time (min)	43(13)	45 (15)
First SBT failure (N)	1	0
PEEP (cmH_2O)	5.4 (0.5)	6 (1.73)
PSV (cmH_2O)	7.3 (0.48)	6.33 (0.57)
FiO_2	0.31 (0.03)	0.3 (0)
RR (rpm)	18.58 (3.96)	22.66 (3.05)
VM (ml)	9.87 (3.9)	11.52(2.3)
TV (ml)	576.01 (178.06)	516.87 (120.14)
RSBI (f/L/mi)	36.38 (15.56)	46.00 (14.60)
PaO_2/FiO_2 (mmHg)	418.44 (89.78)	370.73 (37.07)
MIP (cmH_2O)	46.23 (25.09)	37.33 (15.14)
MIP (% predicted)	32.91 (17.09)	25.57 (6.55)
Use of NIV post extubation (N)	14	3

TOT – tube orotracheal; SBT - spontaneous breathing test; PEEP - positive expiratory end pressure; PSV - pressure support ventilation; FIO_2 – fraction of inspired oxygen; VM - volume per minute; TV – tidal volume; RSBI - rapid shallow breathing index; Pao_2/FiO_2 - oxygenation index; MIP - maximum inspiratory pressure; MIP (%) - percentages of maximum inspiratory pressure predicted; NIV – non-invasive ventilation.

Table 3. clinical data and indexes of the 20 patients evaluated.

Variables	Successful N=17	Failure N=3
	Mean (SD)	Mean (SD)
Hemodialysis (N)	10 (58%)	2 (66%)
Positive Water Balance (ml)	383 (453.96)	1518.92 (2417.6)
Negative Water Balance (ml)	1154.5 (745.10)	906.4 (N/A)
Ph	7.35 (0.06)	7.31 (0.10)
PO_2 (mmHg)	113.65 (27.31)	125.53 (11.12)
HCO_3 (mEq/L)	20.96 (2.59)	17.93 (6.77)
PCO_2 (mmHg)	38.84 (5.12)	35.43 (9.62)
Vasoactive Drugs (N)	0	3
SOFA	4.5(1.9)	3.5(0.7)
SAPS 3	43.82 (13.33)	52.66 (8.50)
Planned SAPS Mortality (%)	0.13 (0.13)	0.23 (0.13)

PO_2 – arterial oxygen pressure; HCO_3 – bicarbonate; PCO_2 - partial pressure of carbon dioxide; SAPS - Simplified Acute Physiology Score.

DISCUSSION

Of the top five indexes recommended by III Brazilian Consensus Mechanical Ventilation, three were used in our study: RSBI, maximum inspiratory pressure (MIP) and minute ventilation (MV). The relation of airway occlusion pressure during the first 100 ms of inspiration (P0,1), was not used by the absence of necessary and specific equipment to its proper measurement, and the index of CROP (complacency, frequency, oxygenation, pressure), also was not used, being considered as a limitation of the study for loss of data on the values of plateau pre extubation pressure. [18.19] All recommended indexes show similar efficiency in assisting the conduct of weaning, confirming our hypothesis that values found when according to normality relate with the greatest chance of the patient remain stable after extubation, except for inspiratory muscle strength (MIP), which, in this study, showed to be less than the predicted value, even in patients who evolved successfully extubation.

Studies show the difficulty of the health professionals to predict the ideal time to start and finish the weaning; this difficulty becomes even more apparent in populations with specific characteristics, as experienced by the kidney transplanted patients. According to Figueroa, the accuracy in finding the exact moment of this process varies around 59%. And the situation of these patients in the first 48 hours is what determines the course of evolution. [20]

Bush studied a group of 80 chronic renal individuals distributed in different levels of severity of the disease. In his findings were not found differences in results regarding spirometry values, however, the group transplanted, the residual volume was lower when compared to other groups with $p<0.01$, which suggests an important commitment probably due to multiple lung infections and surgical approach. [21] This fact could lead us to think that our patients, chronic renal transplant recipients and many of them undergoing hemodialysis sessions would have higher risk of post-extubation failure. However, we observed that only three patients evolved with failure after extubation.

Another probable cause of pulmonary impairment cited by this same author was the respiratory muscle dysfunction, in addition to the reduced lung volume, [22] which would be confirmed in our patients that presented MIP also reduced and may be exacerbated in patients transplanted by the use of immunosuppressive drugs and steroids.

Kovelis assessed lung function and respiratory muscle strength in chronic renal failure patients undergoing hemodialysis, concluding that the worsening of pulmonary function was associated with weight gain in the interdialytic period. This study also shows the decrease in respiratory muscle strength associated with hemodialysis time to which the individual was exposed. [23] Although we have not measured the hemodialysis time, we can infer that the low inspiratory pressures may be related to the hemodialysis sessions, to which these patients underwent in the course of the disease. As well as the use of corticoids and the constant changes in fluid balance which worsens the muscle function and consequently pulmonary of these individuals. [24]

Vieira in his review article notes that individuals with chronic kidney failure are subject to many disturbances and musculoskeletal deformities. According to this author that weakness reaches type II muscle fibers, which can be caused by vitamin D deficiency, peripheral neuropathy, drug toxicity, changes in electrolyte concentrations, in addition to the lack of physical activity. [25] If we infer that these patients may also develop a weakness of the respiratory muscles, we could justify the reduction in rates observed in this study.

Several studies that evaluated chronic kidney patients in situations of weaning of the ventilatory support associated the found failures in the impaired muscle function with MIP, MEP and minute ventilation, vital capacity, inspiratory capacity and low peak flow, anemia in kidney disease which reduces oxygen delivery to the muscles, plus the presence of uremia, poor nutrition, vitamin D metabolism abnormalities, excessive parathyroid hormone, inadequate synthesis of hormone proteins and alteration of the biochemistry integrity of the cell membrane, secondary myopathies to immunosuppressive therapy, water balance, in addition to metabolic abnormalities and immune damage, predisposing infection. [11.26-28]

Santos compared the shallow breathing index in three modes, PSV, CPAP, SBT with T-tube, correlating the results with the success of weaning and, although did not find a significant difference between values confirming the idea that all weaning techniques are safe, the author suggests that the RSBI is able to predict the success, but is not able to predict failure if lower than 105, so it is recommended that be evaluated together with other predictors. [29] In this study we observed that individuals with failed extubation presented higher RSBI, although we couldn't find significant difference, suggests the effectiveness of the index in collaboration with the security of extubation, corroborating with Santos.

Among the various existing studies about weaning of mechanical ventilation and assessment of pulmonary function in kidney individuals we did not find any that evaluated the weaning predictive indices in this specific population. In relation to muscle strength, several studies about inspiratory and expiratory muscles were found and all presented similar results as regards the reduction of the MIP [30] which corroborates with our results that also showed the decrease of MIP and percentage of predicted MIP for this population.

We could also observe that the failed extubation group showed age, BMI and respiratory rate higher compared to the successful group. In addition, it presented metabolic acidosis which may justify the increased respiratory rate by hyperventilation, which can take the patient to the tiredness and muscle fatigue, explaining the lack of success in weaning and extubation. Other factors that could justify the failures

in these patients would be the shortest time of intubation (96 hours) and score higher on the gravity SAPS when compared to the successful extubation group. A shorter intubation can highlight precocity in the retreat of the ventilatory prosthesis, because in this study, even though the indexes evaluated were outside the normal parameters, if the patient were in satisfactory clinical condition and level of consciousness the extubation would be held.

We highlight as limitations of the study the sample loss, the number of extubations that occurred before the 24-hour period, and the adherence of the team about the implementation of the protocol, even if previously trained.

Considering the observed results, this study opens up spaces for conducting a longitudinal study with this population, in which we can associate the weaning predictive indexes with the time of exposure to dialysis which the patients were submitted, obtain a cutting point for the studied indexes using a larger sample, and also take advantage of more recent studies that suggest the importance of individualized data such as anthropometric values [32] and markers of cardiac dysfunction [33] of the patients in the construction of predictive indexes.

CONCLUSION

In this pilot study, the weaning predictive indexes of mechanical ventilation commonly used for the general population, when within the expected values of normality, do not appear to be sensitive in predicting successful extubation in renal transplant patients, but in general practice it showed to be safe and efficient in helping the team in the weaning process with an appropriate clinical evaluation.

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AUTHOR'S CONTRIBUTIONS

Silva, LDA – collect, data creation and acquisition and writing of the manuscript
Almeida, MMMF - collect, statistical analysis and writing of the manuscript
Quaresma, MO – collect and data acquisition
Castro, T – collect and data acquisition
Santos, AM – collect and data acquisition
Chiavegato, LD – delineation and main guidance of the study, statistical analysis and final revision of the manuscript

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest in the research.

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