Correlations of Egen Klassifikation and Barthel Index scores with pulmonary function parameters in Duchenne muscular dystrophy

Marisa Afonso Brunherotti, PT, MSc,[a] Claudia Sobreira, MD, PhD,[b]
Antônio Luiz Rodrigues-Júnior, DDS, PhD,[c] Marcos Renato de Assis, MD, PhD,[d]
João Terra Filho, MD, PhD,[a] and José Antônio Baddini Martinez, MD, PhD[a]

PURPOSE: This study investigated the correlations obtained by using the Egen Klassifikation (EK) and Barthel Index (BI) functional scales and respiratory function parameters in patients with Duchenne muscular dystrophy.

METHODS: Spirometry, maximal respiratory pressures, and arterial blood gases were analyzed and graded according to the EK and BI scales in 26 patients. They were classified as high or low risk for introduction of noninvasive ventilation according to the respiratory function.

RESULTS: The EK and BI scales significantly correlated with forced vital capacity, forced expiratory volume in 1 second, and maximal respiratory pressures. The worse the functional performance, the worse the respiratory measurements. The degree of correlation between the functional scales and each respiratory parameter was similar. An EK of 21 or higher predicted high risk for the introduction of noninvasive ventilation.

CONCLUSIONS: EK and BI scales similarly correlated with the degree of respiratory involvement in Duchenne muscular dystrophy. The EK scale was superior in detecting subjects with a higher risk for introduction of noninvasive ventilation. (Heart Lung® 2007;36:132–139.)

Duchenne muscular dystrophy (DMD) is a disease caused by mutation of the dystrophin gene, characterized by progressive loss of muscle strength.[1,2] The disease usually involves the proximal muscle groups, and the ability to ambulate is lost at approximately 9 years of age. The respiratory muscles also become sick; the most common cause of death is respiratory failure and related complications. Recent advances in respiratory care involving noninvasive mechanical ventilation and airway clearance devices have improved the outcome for these patients.[1,3,4]

Functional assessment scales have been used in DMD for decades as a common frame of reference for planning and evaluating rehabilitative interventions by specialists. Several tools have been used in this setting, including those developed by Swinyard et al,[5] Vignos et al,[6] and Brooke et al,[7] and the Barthel Index (BI).[8] Although these instruments were designed to evaluate functional impairment caused by peripheral muscle dysfunction, a correlation between worse functional classes and reduced forced vital capacity (FVC) and total lung capacity has been suggested.[9-11]

More recently, an additional instrument was developed to evaluate the functional status of patients with advanced DMD and spinal muscular atrophy.[12,13] The Egen Klassifikation (EK) scale (Egen

From the [a]Pulmonary Division, Internal Medicine Department; [b]Neurology, Psychiatrics, and Medical Psychology Department; [c]Social Medicine Department; and [d]Clinics Hospital, Medical School of Ribeirão Preto, University of São Paulo, São Paulo, Brazil.

Klassifikation translation from Danish: "our own classification") was designed to reflect the progressive loss of physical ability for 10 main tasks: (1) control an electric chair, (2) transfer from the wheelchair, (3) stand, (4) sit up, (5) use the arms, (6) use the arms for eating, (7) turn in bed, (8) cough, (9) talk, and (10) general well-being. The last three components of this scale reflect, to some extent, the severity of respiratory failure.

The total score on the EK scale significantly correlated with FVC in groups of patients with DMD and spinal muscle atrophy.[12,13] When the analysis was restricted to DMD, additional significant correlations with forced expiratory volume in 1 second (FEV$_1$), peak expiratory flow, and arterial blood gases were observed. The EK score also showed a higher number of significant correlations, and better coefficients, with respiratory variables, than the European Alliance of Muscular Dystrophy Association scoring system. In DMD, initial EK scores higher than 20 were associated with the need for mechanical ventilation in the following 18 months. These results suggest that the EK scale has properties that better reflect respiratory impairment in DMD than other functional scales.

The objective of this study was to compare the correlations obtained by using the EK scale and a standard measure of physical disability, the BI, with FVC, FEV$_1$, FEV$_1$/FVC ratio, maximal respiratory pressures, and arterial blood gases in a sample of patients with DMD. We also investigated a potential role for these scales in detecting patients with a high risk for introduction of mechanical ventilation.

METHODS
Subjects

Twenty-nine male subjects with a diagnosis of DMD were invited to participate in the study. The patients and their parents were approached in the Pulmonary Function Laboratory just before regular respiratory evaluation for their condition. The diagnosis of DMD was established by the specialized center in neuromuscular diseases of the neurology department in our institution. The diagnosis was established on the basis of clinical grounds, electromyography patterns, and muscle biopsies. Three of the 29 subjects (aged 7, 9, and 23 years) were not included in the study because they were unable to perform acceptable spirometric curves. The study group consisted of 26 subjects with a mean age of 12.7 ± 4.0 years (range: 7–22 years). The protocol was approved by the local ethics committee, and all parents or persons responsible for the patients signed informed consent forms. All protocol evalua-

tions were performed on the same occasion for each patient.

Functional assessment scales

An English version of the EK scale was obtained and translated into the Portuguese spoken in Brazil by the authors. The EK sum score ranges from 0 to 30, with higher scores meaning worse functional performance (Appendix).[13] Although the EK scale has been designed to evaluate non-ambulatory subjects, the present study also included some patients who were still able to walk. In this setting, the best available functional scores were assigned to the questions dealing with wheelchair control.

A Portuguese version of the BI was selected from a previously published study.[14] The BI ranges from 0 to 100, with higher scores meaning better functional status.[15] The same researcher (M.A.B.) applied both functional scales to all subjects. The parents or persons responsible for the patients selected the responses when the patients were unable to answer the questions in a satisfactory manner.

Pulmonary function evaluation

Measurements of FVC and FEV$_1$ were made using a calibrated Pulmonet III spirometer (Sensormedics, Anaheim, Calif), and the FEV$_1$/FVC ratio was calculated. The measurements were performed with the subjects in the sitting position according to the technical recommendations of the American Thoracic Society.[16] The results of FVC and FEV$_1$ were expressed as percentage of the reference values of Knudson et al.[17] Age, sex, and height were used to calculate the reference values. In patients with severe scoliosis, the height was calculated from the maximal horizontal arm span.[18]

Maximal inspiratory pressure (MIP) and maximal expiratory pressure (MEP) were obtained with an analog manovacuometer (MPG Inc, Marshalltown, IA). MIP was measured from the residual volume, just after a maximal expiratory maneuver. MEP was measured from the total lung capacity, immediately after a full inspiration. The best values obtained after three expiratory or inspiratory maneuvers showing less than 10% variation were selected. The results were expressed as the percentage of the predicted values according to the equations of Wilson et al.[19]

With the patients breathing room air, arterial blood samples were collected from the radial artery and immediately measured with a Corning blood gas analyzer model 175 (New York, NY). All pulmonary function tests and blood gas analyses were performed at approximately the same time in the early afternoon.

Risk for introduction of noninvasive ventilation

To evaluate whether the functional scales could show a predictive value for the need of introduction of noninvasive ventilation, the subjects were classified into a low-risk or high-risk group. A subject was considered to be of "high risk for mechanical ventilation" when he satisfied at least one of the following criteria: FVC less than 40% predicted, MIP less than 60% predicted, and $PaCO_2$ of 45 mm Hg or greater.

Statistical treatment

All results are expressed as means and standard deviations. Correlations between the scores of functional scales and respiratory parameters were calculated using Pearson's coefficients. Comparisons between the Pearson correlation coefficients obtained using the two functional scales and the same respiratory parameter were performed with the F test.[20] A P value less than .05 was chosen as the level of significance.

A logistic regression model was applied to determine scores of the functional scales predictive of high risk for introduction of noninvasive ventilation, after classification of the subjects according to the above criteria.[21] Once the mathematic expressions were obtained, the functional scores predictive of high risk for introduction of mechanical ventilation, with a probability of 90%, were calculated.

RESULTS

Nineteen (73.1%) of the subjects were wheelchair dependent. Only one of the subjects was using nocturnal noninvasive ventilation, and his blood gas measurements were not included in the present analysis. Although the individual degree of functional dysfunction evaluated by the scales was diverse, the group as a whole may be classified as showing light to moderate functional impairment (Table I). A substantial amount of variation was also observed in all pulmonary function parameters. The mean group values showed a discrete decrease in MIP and a more pronounced reduction in MEP. The group may also be classified as having mild to moderate restrictive ventilatory insufficiency, and their mean arterial blood gases were within the normal range.

The EK scale showed statistically significant positive correlations with age and significant negative correlations with FVC, FEV_1, MIP, and MEP (Table II). The BI exhibited statistically significant inverse correlations with age and the FEV_1/FVC ra-

Table I
Functional scales and respiratory function parameters for 26 patients with Duchenne muscular dystrophy

	EK Sum	Barthel Index	FVC (% predicted)	FEV_1 (% predicted)	FEV_1/FVC (%)	MIP (% predicted)	MEP (% predicted)	pH+	PaO2* (mm Hg)	PaCO2+ (mm Hg)
Mean ± SD	8.1 ± 7.3	54.0 ± 26.2	62.8 ± 23.4	62.4 ± 22.3	87.0 ± 7.9	75.4 ± 23.7	63.2 ± 39.6	7.44 ± 0.02	88.6 ± 6.9	37.1 ± 3.4
Range	0–23	20–95	14.0–94.9	13.8–97.0	64.1–98.2	33.9–132.2	19.8–200.0	7.39–7.49	64.0–99.5	30.4–45.5

EK, Egen Klassifikation; *FVC*, forced vital capacity; *FEV₁*, forced expiratory volume in 1 second; *MIP*, maximal inspiratory pressure; *MEP*, maximal expiratory pressure; *SD*, standard deviation.
*Results for 25 subjects.

Table II
Pearson's correlation coefficients (r) between functional scales and respiratory function parameters for 26 patients with Duchenne muscular dystrophy

	Age	FVC (% predicted)	FEV$_1$ (% predicted)	FEV$_1$/FVC (%)	MIP (% predicted)	MEP (% predicted)	pH*	PaO$_2$* (mm Hg)	PaCO$_2$* (mm Hg)
EK Sum	0.596†	−0.751†	−0.665†	0.372	−0.674†	−0.521†	0.0220	−0.0262	0.0364
Barthel Index	−0.512†	0.679†	0.556†	−0.482†	0.562†	0.442†	−0.0451	0.0064	−0.0188

EK, Egen Klassifikation; *FVC*, forced vital capacity; *FEV*, forced expiratory volume in 1 second; *MIP*, maximal inspiratory pressure; *MEP*, maximal expiratory pressure.

*Results for 25 subjects.

†p < 0.05.

tio, and positive correlations with FVC, FEV$_1$, MIP, and MEP. The functional scales did not show significant correlations with the arterial blood gases. Comparisons between the Pearson's correlation coefficients obtained using the two functional scales and each respiratory parameter, performed by the F test, did not show any statistically significant difference (Table II).

Eleven subjects were classified as having a high risk for introduction of noninvasive ventilation. Logistic regression models were developed to calculate the probability of a subject to be classified as being at high risk for noninvasive ventilation on the basis of his or her functional scale scores (Table III). It was not possible to determine a BI score predictive of high risk for noninvasive ventilation with at least a 90% probability (Fig 1A). EK scores equal to or higher than 20.7 predicted high risk for noninvasive ventilation with 90% probability and 40% specificity (Fig 1B).

DISCUSSION

The present study showed that both the EK and BI functional assessment scales significantly correlate with spirometry and respiratory muscle strength measurements in patients with DMD. The degree of such correlations was similar because the correlation coefficients between the two scales and each respiratory parameter did not significantly differ. Furthermore, an EK score equal to or higher than 21 seems to predict a high risk for the need of noninvasive ventilatory support.

DMD is an illness characterized by progressive loss of muscle strength, leading to loss of ambulation and death, most frequently from respiratory failure. A continuously progressive restrictive pulmonary syndrome becomes apparent by 10 to 12 years of age and results in respiratory insufficiency during the second or third decade of life.[1,22] Although the respiratory muscle weakness is a major component of this process, simultaneous progressive spinal deformity frequently contributes to the respiratory deterioration.[1,23]

Because the disease strikes all striated muscles, some degree of correlation between peripheral and respiratory muscle dysfunction may be expected. Paravertebral muscle weakness also contributes to scoliosis and thoracic deformity. In this setting, functional abilities and respiratory function will deteriorate simultaneously. This fact is a common observation made by health professionals involved in the care of these subjects, and former investigations have already addressed this

Table III

Parameter estimates and predictive property values for the univariate logistic model risk of mechanical ventilation versus functional scales

Scale	Constant	Slope	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value
EK Sum	−1.3754	0.3122	0.8125	0.6000	0.7647	0.6667
Barthel Index	4.4436	−0.0689	0.7500	0.7000	0.8000	0.6364

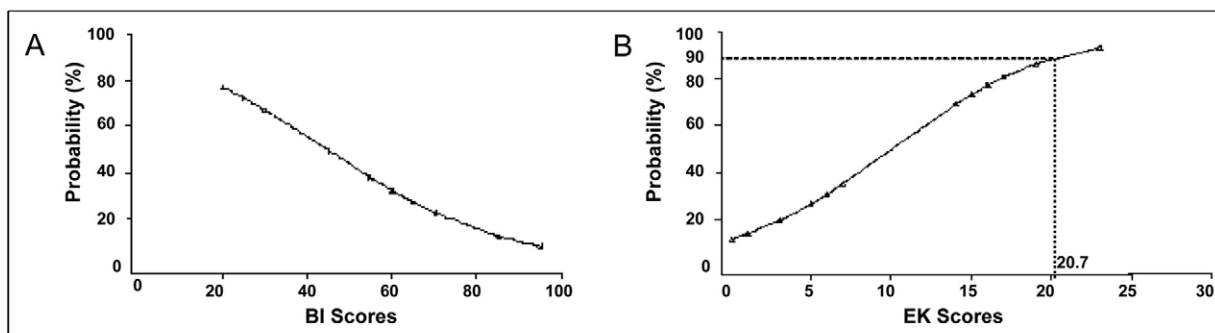*EK*, Egen Klassification.

Fig 1 Logistic regression models showing the relations between the probability of "high risk for introduction of mechanical ventilation" and scores of the scales BI (A) and EK (B). *BI*, Barthel Index; *EK*, Egen Klassifikation.

issue. Previous studies investigated the presence of correlations between some functional assessment scales, such as the scale of Vignos and pulmonary function parameters.[9-11] Although statistical analysis was poor or absent, these investigations strongly suggested a relationship between worse functional classes and pulmonary function deterioration.

Clear, statistically significant correlations between worse respiratory parameters and a general functional scale have been described only for the EK scale in a small group of patients with DMD and spinal muscular atrophy.[12] Because this scale incorporates three questions that may reflect respiratory dysfunction (coughing, talking, and well-being), it may be superior to other functional measurements in detecting the presence of respiratory failure. We compared the EK scale with the BI because the latter tool has been used in several chronic disabling conditions for a long time, and it has already been extensively tested regarding its confidence and validity.[15]

Both functional scales showed statistically significant linear correlations in the expected directions with the patients' age because the older the subjects, the more severe their overall condition. Similar correlations were observed between the scales and FVC, FEV_1, MIP, and MEP, indicating that the worse the functional abilities, the worse the pulmonary restrictive defect and respiratory muscle strength. The BI also showed a significant inverse correlation with the FEV_1/FVC ratio. This last finding is probably explained by the presence of more severe pulmonary restriction in patients with more advanced DMD. Decreases in thoracic and lung compliance caused by respiratory muscle dysfunction and thoracic deformities would increase the expiratory flow and the FEV_1/FVC ratio. The reasons for the statistically significant correlation of the FEV_1/FVC ratio observed only with the BI and not with the EK scale still remain to be explained.

There were no statistically significant correlations between arterial blood gases and either functional scale. This occurred because almost all pa-

tients showed normal blood gases. We can guess that despite the presence of respiratory restriction and muscle weakness, the diaphragm is able to keep adequate diurnal ventilation in DMD for a long time. Indeed, carbon dioxide retention in awake patients has been associated only with FEV_1 values of less than 20%.[24] We may also assume that the low level of physical activity of these patients leads to small oxygen consumption and carbonic gas production, contributing to this finding.

The treatment of hypoventilation with noninvasive ventilation can improve gas exchange and prolong survival in patients with DMD.[1,3,4] Various levels of impairment of pulmonary function and gas exchange have been reported to be associated with an increased risk of respiratory complications and death.[1,24-26] Although the presence of awake carbon dioxide retention is a mandatory indication for noninvasive ventilation, poor 2- to 3-year survival has also been seen in patients with $Paco_2$ within normal limits.[1,25,26,27] In the last situation, the investigation of sleep-related hypoventilation events is important.[1,24,25,28] However, sleep studies in patients with DMD may be troublesome, because the subjects often show skeletal deformities and locomotion limitations. In addition, sleep studies are expensive tests and not always easily available in developing countries. One study already reported that an FEV_1 of less than 40% and an awake $Paco_2$ of 45 mm Hg or higher are sensitive, although nonspecific, indicators of sleep hypoventilation.[24]

Because our results indicate that functional scales linearly correlate with the degree of pulmonary dysfunction, we could guess that their scores might help evaluate the risk for introduction of noninvasive ventilation. Thus, on the basis of previously published data, we chose a set of parameters that permitted us to classify the patients according to their risk of requiring noninvasive ventilation.[24,29,30] Although this approach was not ideal, a logistic regression model indicated that an EK score of 21 or higher is associated with a 90% probability of being included in the high-risk group. A similar score could not be determined for the BI. Nonsignificant findings for the BI may be the consequence of the small number of patients enrolled in the study. However, we should also consider that the EK scale truly exhibits better properties for reflecting respiratory status than the BI. The inclusion of questions dealing with the ability to cough and talk, and well-being in the EK scale, not included in the BI scale, might be responsible for this difference.

The determination of a functional scale score able to indicate an elevated risk for need of noninvasive ventilation has clinical meaning. The periodic application of the EK scale by health professionals may detect a point when more intensive respiratory monitoring and additional studies including sleep studies will be necessary. This scale could then be considered as a simple, practical, and inexpensive method for monitoring respiratory function in patients with DMD.

CONCLUSION

Although both the EK and BI scales exhibited significant correlations with respiratory function parameters in DMD, the former was superior in detecting subjects with higher risk for introduction of noninvasive ventilation. Additional studies exploring correlations between EK scale scores and sleep study parameters are necessary. Prospective investigations involving repeated EK scale measurements and their relation with the moment of introduction of noninvasive ventilation are also required.

APPENDIX

The Egen Klassifikation scale

Each category consists of four items (0–3), and the Egen Klassifikation total score is the sum of scores over categories.

1. Ability to use wheelchair
   0. Able to use a manual wheelchair on flat ground, 10 m in less than 1 minute.
   1. Able to use a manual wheelchair on flat ground, 10 m in more than 1 minute.
   2. Unable to use manual wheelchair, requires electric wheelchair.
   3. Uses electric wheelchair, but occasionally has difficulty in steering.

2. Ability to transfer from wheelchair
   0. Able to transfer from wheelchair without help.
   1. Able to transfer independently from wheelchair with use of aid.
   2. Needs assistance to transfer with or without additional aids (lift, easy glide).
   3. Needs to be lifted with support of head when transferring from wheelchair.

3 Ability to stand
   0. Able to stand with knees supported, as when using braces.
   1. Able to stand with knees and hips supported, as when using standing aids.
   2. Able to stand with full body support.

3. Unable to be stood, marked contractures.

4. Ability to balance in the wheelchair
   0. Able to push himself upright from complete forward flexion by pushing up with hands.
   1. Able to move the upper part of the body more than 30 degrees from the upright position in all directions, but cannot push himself upright from the total forward flexed position.
   2. Able to move the upper part of the body less than 30 degrees from one side to the other.
   3. Unable to change position of the upper part of the body, cannot sit without total support of trunk and head.

5. Ability to move the arms
   0. Able to raise the arms above the head with or without compensatory movements.
   1. Unable to lift the arms above the head, but able to raise the forearms against gravity, ie, hand to mouth with or without elbow support.
   2. Unable to lift the forearms against gravity, but able to use the hands against gravity when the forearm is supported.
   3. Unable to move the hands against gravity but able to use the fingers.

6. Ability to use the hands and arms for eating
   0. Able to cut meat into pieces and eat with spoon and fork. Can lift a filled cup (~250 mL) to the mouth without support at elbow.
   1. Eats and drinks with support at elbow.
   2. Eats and drinks with elbow support and with reinforcement of the opposite hand ± feeding aids.
   3. Has to be fed.

7. Ability to turn in bed
   0. Able to turn himself in bed with bedclothes.
   1. Able to turn himself on a couch, but not in bed.
   2. Unable to turn himself in bed. Has to be turned three times or less during the night.
   3. Unable to turn himself in bed. Has to be turned four times or more during the night.

8. Ability to cough
   0. Able to cough effectively.
   1. Has difficulty to cough and sometimes needs manual reinforcement. Able to clear the throat.
   2. Always needs help for coughing. Only possible to cough in certain positions.
   3. Unable to cough. Needs suction and/or hyperventilation techniques or intermittent positive-pressure breathing to keep the airways clear.

9. Ability to speak
   0. Powerful speech. Able to sing and speak loudly.
   1. Speaks normally, but cannot raise his voice.
   2. Speaks with quiet voice and needs a breath after three to five words.
   3. Speech is difficult to understand except to close relatives.

10. Physical well-being
    0. No complaints, feels good.
    1. Easily tires. Has difficulty resting in a chair or in bed.
    2. Has loss of weight, loss of appetite. Scared of falling asleep at night, sleeps badly.
    3. Experiences additional symptoms such as change of mood, stomach ache, palpitations, perspiring.

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