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The Suitability of Models to Prefigure Organic Functions and to Avoid Item Dispersion of a Variable Indexing on Height Rather than BSA Shown by Comparing Two Studies

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Abstract— **A previous study based on theoretical data on the glomerular filtration rate evaluated the effect of different indexations on the distribution of the indexed values versus the distribution of the non-indexed values; this study showed that the lowest dispersion of values was due to indexation based on height. Consequently, we planned to confirm these theoretical results by comparing them to a parallel study based on the values of the clearance of creatinine in a real population of patients undergoing peritoneal dialysis. This study showed a very strong correlation between the results of the theoretical study and the study of the real population, thus demonstrating the suitability of this preliminary approach for research using theoretical models to preview and confirm the results of a study using a real population.**

Index Terms— Models Comparison, Indexation, GFR, CTCL

I. PREMISE

The most used method of indexation of the values of organic functions is based on Body Surface Area (BSA) according to the following formula: value n x 1.73 m^2/BSA m^2, where 1.73 m^2 is the reference BSA adopted in 1928, which has never been modified until now, and BSA m^2 is the BSA of the individuals whose values of organic functions have to be indexed. This system may frequently result in misrepresentation of the indexed items, as emphasized by many studies in this field [1-6]. It seems useful to remind us that these warped evaluations may arise from different causes inherent in the formulas proposed for BSA estimation, beginning with the inadequate selection of people from which the reference body surfaces measures were collected [5] to the very possible change over time in the weight of the individuals whose BSA has to be estimated, which is frequently an increase. Weight is a body dimension included in all the suggested formulas, and its increase will result in an increase in BSA previously estimated to be lower. This difference will cause a decrease in the indexed function, notwithstanding that the measured value could be unmodified, a result to be accepted only in the case that the increase in the weight is due to an increase in muscle mass. Taking into account the high possibility of errors due to what is specified above, it was proposed that we should index based on height [7], a body dimension subjected only to a marginal decrease over time due to aging [8]. The eventual significant modification over time of height, due to pathologies of the spine, have to be neglected because the height to be considered for indexation is the baseline height, which is the height achieved at the end of the growth, because of its association with muscle mass, with the size of the organs and consequently with the organs' functions. A different possible effect of indexing a variable is the modification of the distribution of its items, an event to be expected as more probable when indexing on BSA based on the above-mentioned findings. The wide variability in the height/weight ratio in a series of subjects whose measured values are indexed can induce a significant distortion in the distribution of the measured values, inducing a strong and very warped modification of the relationship between measured and indexed values. This distortion will have negative effects when comparing organic functions between two groups of individuals or when carrying out a regression between the data of the groups, probably resulting in questionable conclusions. The indexation based on height could avoid such problems because height is a non-questionable body measure due to its marginal change over time, while its eventual and significant pathological modification does not affect the indexation. The usefulness of indexing based on height and the preservation of the item distribution of the measured values was evaluated in a previous paper [9] and based on a theoretical model that studied the effect of different indexations on normal and decreased glomerular filtration rates (GFRs) of 100 males and 100 females. Decreased GFRs were obtained by a random coefficient of correction of the normal GFRs. All the data in the model were created using MINITAB 15, Minitab Inc.; State College, PA, USA. This model was named " Model" in the present text. The quoted research concluded that the lowest dispersion of data was attained by the indexation based on height. The limitation of the Model was based on theoretical subjects and not on a real population. Consequently, the aim of this study was to verify the suitability of the Model results, comparing the Model to real population data. This study consisted of 45 males and 94 females with end stage renal disease and undergoing peritoneal dialysis (PD). In the present study, all the elaborations and analyses concerning the decreased GFRs in the Model were similarly found with creatinine clearance, and the results of the two studies were compared. For the aim of

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the present study, the data on the decreased GFRs instead of those with normal GFRs were selected for the Model because their range was closer to the range of the creatinine clearance data. This better relationship was evaluated by the percentage difference between the data: males, decreased GFR versus CtCl/min 0.156 %, normal GFR versus CtCl/min 75.21 %; and females, decreased GFR versus CtCl/min 25.79 % , normal GFR versus CtCl/min 63.79 % The verification of an actual correspondence between the results from the Model and the results from the study on creatinine clearance strengthen the usefulness of the Model because the degree of its effectiveness was verified, a result of particular interest in the case of positive correspondence for indexations based on height.

II. Methods

According to the argument above, the data on creatinine clearance in males and females underwent the same elaborations and statistical analyses as those performed in the Model for the data on the randomly decreased GFRs. The results of the Model are shown in tables of data that can be compared with the tables of data on CtCl/min. The tables are located in the text following one another to allow a direct comparison of the data. The following statistical analyses were performed: A) descriptive statistics for males and females, such as the mean, standard error of the mean, trimmed mean, standard deviation, variance, coefficient of variation, median, and skewness that are reported in tables 1, 2, 3, and 4. B) Regressions between the following data of the two studies: 1) the means of CtCl/min and of its indexations based on BSA by DuBois, Haycock, Lee and its indexation based on height versus the means of decreased GFR and its consistent indexations, 2) the skewness of CtCl/min and the consistent indexations versus the skewness of GFR and its consistent indexations, and 3) the coefficient of variation of CtCl/min and the consistent indexations versus the coefficient of variation of GFR and the consistent indexations. The results of the regressions are shown in table 5 for males and females. C) The comparison, using regressions, of the relationship between indexed and non-indexed decreased GFRs and between indexed and non-indexed CtCl/min. The comparison of results of the regressions was based on a comparison of their percentage residuals, statistically obtained with a 2-sample T-tests, see tables 5 -11. D) A study of the relationships of variance, skewness and coefficients of variation between GFRs based on the Model and CtCl/min. Statistical analysis using regressions to compare the degree of dispersion of their items was conducted, and the results are reported in tables 12A and 12B.

III. Results

Tables 1A and 1B contain, respectively, the descriptive statistics of the non-indexed CtCl/min and its indexations for 45 male patients undergoing PD and the decreased GFR and its indexations from 100 theoretical male subjects using the Model. Tables 2A and 2B show the descriptive statistics of CtCl/min and its indexations from 94 females undergoing PD and the decreased GFR and its indexations from 100 theoretical females using the Model.

Tab. 1A - Descriptive statistics of 45 male patients undergoing PD and consistent different indexations

Variables	Mean	SE Mean	TrMean	StDev	Variance	CoefVar	Median	Skewness
CtCl/min	8,638	0.391	8.541	2.62	6.865	30.33	8.344	0.61
CtCl/min/index. Du Bois	7.977	0.327	7.925	2.194	4.812	27.5	7.48	0.44
CtCl/min index. Haycock	7.842	0.329	7.786	2.209	4.878	28.16	7.4178	0.45
CtCl/min index. Lee	7.817	0.32	7.766	2.15	4.621	2.,5	7.33	0.44
CtCl/min index. Height	5.078	0.213	5.038	1.14	2.046	28.17	4.676	0.56

Tab. 1B - Descriptive statistics of 100 decreased male GFRs and consistent different indexations

Variable	Mean	SE Mean	TrMean	StDev	Variance	CoefVar	Median	Skewness
GFR	59.97	0.543	59.94	5.43	29.5	9.06	60.5	0.04
GFR indexed Du Bois	56.43	0.545	56.33	5.45	29,71	9.66	56.64	0.27
GFR indexed Haycock	56.65	0.545	56.52	5,45	29.7	9.62	56.53	0.37
GFR indexed Lee	55.3	0.534	5.,2	5.34	28.53	9.66	55.5	0.27
GFR indexed Height	34.16	0.329	34.14	3.29	10.84	9.63	36.76	-0.01

Tab. 2A - Descriptive statistics of 94 female patients undergoing PD and consistent different indexations

Variables	Mean	SE Mean	TrMean	StDev	Variance	CoefVar	Median	Skewness
CtCl/min	8.046	0.235	8.002	2.283	5.213	28.38	8.224	0.13
CtCl/min/index. Du Bois	8.522	0.231	8.509	2.237	5.002	26.24	8.722	-0.01
CtCl/min index. Haycock	8.359	0.225	8.349	2.183	4.764	26.11	8.606	-0.01
CtCl/min index. Lee	8.352	0.226	8.339	2.192	4.804	26.24	8.547	-0.01

CtCl/min index. Height	5.09	0.145	5.071	1.405	1.974	27.6	5.268	0.06

Tab. 2B - Descriptive statistics of 100 decreased female GFRs and consistent different indexations								
Variables	Mean	SE Mean	TrMean	StDev	Variance	CoefVar	Median	Skewness
GFR	55.4	0.496	55.369	4.962	24.618	8.96	54.55	0.14
GFR Indexed Du Bois	57.521	57.085	57.323	7.133	50.879	12.4	57.065	0.36
GFR indexed Haycock	57.345	0.699	57.168	6.691	6.691	11.67	44.766	0.33
GFR indexed Lee	56.368	0.699	56.174	6.99	48.859	12.4	55.921	0.36
GFR indexed Height	33.57	0.371	33.476	3.709	11.396	11.05	33.04	0.29

The regression of the means, the skewness, and the coefficients of variation of CtCl/min and its indexations versus the corresponding data by the Model verified their consistency.

Regressions of means, skewness, and coefficients of variation of CtCl/min versus the same data of GFRs by the Model		Statistics of the regressions		
Tab. 3A Males	Variables	R	R^2	P
predictor	Means of GFR and indexed GFRs			
response	Means of CtCl/min and indexed CtCl/min	0.996	0.991	0.000
predictor	Skewness of GFR and indexed GFRs			
response	Skewness of CtCl/min and indexed CtCl/min	0.9	0.811	0.037
predictor	Coeff. Var. of GFR and indexed GFRs			
response	Coeff. Var of CtCl/min and indexed CtCl/min	0.975	0.951	0.0046

Regressions of means, skewness, and coefficients of variation of CtCl/min versus the same data of GFRs by Model		Statistics of the regressions		
Tab. 3B Females	variables	R	R^2	P
predictor	Means of GFR and indexed GFRs			
response	Means of CtCl/min and indexed CtCl/min	0.998	0.997	0
predictor	Skewness of GFR and indexed GFRs			
response	Skewness of CtCl/min and indexed CtCl/min	0.968	0.937	0.0068
predictor	Coeff. Var. of GFR and indexed GFRs			
response	Coeff. Var of CtCl/min and indexed CtCl/min	0.926	0.857	0.024

The tables above clearly show the strong correlation existing between the descriptive data from the Model and the descriptive data of CtCl/min. The following step concerns the comparison of the relationship between non-indexed and indexed GFRs in the Model and in the CtCl/min. The related data are shown in tables 4, 5, and 6 for males and in tables 7, 8, and 9 for females. These tables show comparisons of the regressions of indexed GFRs vs non-indexed GFRs and the corresponding regressions with CtCl/min. Their results were compared analyzing the differences between their residuals. The comparisons in tables 4 and 5 are shown in table 6. The differences were evaluated by T-test and point to a difference in the indexation by Haycock, in males and in females, as shown in tables 7, 8, and 9. Tables 7-9 report the comparison, by T-test, of the percentage residuals of the regressions shown in tables 3A and 3B.

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	Tab. 4 - 100 males with decreased GFRs - Linear regressions of indexed GFRs vs non-indexed GFRs					
	Statistics of the regressions					
	Predictor	Responder	R	R^2	P	% absolute residuals mean ± SD
A	non-indexed GFR	indexed DuBois	0.808	0.654	0.000	5.48±3.67
B	non-indexed GFR	indexed Haycock	0.836	0.699	0.000	5.029±3.24
C	non-indexed GFR	indexed Lee	0.809	0.654	0.000	5.48±3.67
D	non-indexed GFR	indexed height	0.867	0.753	0.000	4.17±2.92
	Tab. 5 - 45 Males - Linear regressions of indexed CtCl/min vs non-indexed CtCl/min					
	Statistics of regressions					
	Predictor	Responder	R	R^2	P	% absolute residuals mean ± SD
a1	non-indexed CtCl/min	indexed DuBois	0.966	0.933	0.000	6.31±3.85
b1	non-indexed CtCl/min	indexed Haycock	0.956	0.913	0.000	7.32±4.11
c1	non-indexed CtCl/min	indexed Lee	0.966	0.933	0.000	6.31±3.85
d1	non-indexed CtCl/min	indexed height	0.986	0.972	0.000	3.74±2.43

Tab 6 – Males - Comparison of regressions	
T-test of Tab. 4 residuals % vs Tab. 5 residuals %	
a versus a1	T-Value = 1.22 P-Value = 0.227 DF = 81
b versus b1	T-Value = 3.31 P-Value = 0.002 DF = 69
c versus c1	T-Value = 1.22 P-Value = 0.227 DF = 81
d versus d1	T-Value = -0.92 P-Value = 0.358 DF = 100

	Tab. 7 - Females with decreased GFRs - Linear regressions of indexed GFRs vs non-indexed GFRs					
	Statistics of regressions					
	Predictor	Responder	R	R^2	P	% absolute residuals mean ± SD
a1	non-indexed GFR	indexed DuBois	0.799	0.638	0.000	5.92±4.02
b1	non-indexed GFR	indexed Haycock	0.819	0.67	0.000	5.54±3.69
c1	non-indexed GFR	indexed Lee	0.799	0.638	0.000	5.92±4.03
d1	non-indexed GFR	indexed height	0.875	0.767	0.000	4.18±2.84
	Tab. 8- Females - Linear regressions of indexed CtCl/min vs non-indexed CtCl/min					
	Statistics of regressions					
	Predictor	Responder	R	R^2	P	% absolute residuals mean ± SD
A	non-indexed CtCl/min	indexed DuBois	0.839	0.881	0.000	7.14±5.14
B	non-indexed CtCl/min	indexed Haycock	0.929	0.864	0.000	7.34±5.35
C	non-indexed CtCl/min	indexed Lee	0.939	0.881	0.000	7.14±5.14
D	non-indexed CtCl/min	indexed height	0.984	0.969	0.000	4.03±2.67

Tab 9 - Females- Comparison of regressions T-test of Tab. 8 residuals % vs Tab. 9 residuals %	
a versus a1	T-Value = 1.83 P-Value = 0.068 DF = 176
b versus b1	T-Value = 2.71 P-Value = 0.007 DF = 163
c versus c1	T-Value = 1.83 P-Value = 0.069 DF = 176
d versus d1	T-Value = -0.38 P-Value = 0.705 DF = 191

Tab. 10A - Males - Descriptive statistics of % residuals of regressing indexed GFRs versus non-indexed GFRs compared with the % residuals of regressing indexed ClCls/min versus non-indexed ClCls/min

Indexation from DuBois

	Mean	StDev	Minimum	Median	Maximum	Range
GFRs	5.48	3.67	0.043	5.22	15.5	15.46
CtCls	6.31	3.85	0.184	5.81	14.41	14.23
Diff %	-15.01	-27.49	-328	-11.3	7.024	7.96

Tab. 10A Males **-** Indexation from Haycock

	Mean	StDev	Minimum	Median	Maximum	Range
GFRs	5.029	3.24	1.15	4.87	13.76	13.61
CtCls	7.324	4.12	0.23	7.24	15	14.77
Diff %	**-45.6**	**-44.4**	80	-48.6	-9.035	-8.58

Tab. 10A Males - Indexation from Lee

	Mean	StDev	Minimum	Median	Maximum	Range
GFRs	5.48	3.67	0.043	5.22	15.5	15.46
CtCls	0.307	3.85	0.184	5.81	14.41	14.23
Diff %	-4.96	-27.49	-6.3	-11.3	7.024	7.96

Tab. 10A Males - Indexation on Height

	Mean	StDev	Minimum	Median	Maximum	Range
GFRs	3.74	2.44	0.076	3.52	10.18	10.11
CtCls	4.17	2.802	0.16	3.73	10.74	10.58
Diff %	***-11.7***	***-14.8***	-110.5	-6.05	-5.48	-4.68

Tab. 10B - Females - Descriptive statistics of % residuals of regressing indexed GFRs versus non-indexed GFRs compared with the % residuals of regressing indexed ClCls/min versus non-indexed ClCls/min

10B Females - Indexation on DuBois

	Mean	StDev	Minimum	Median	Maximum	Range
GFRs	5.85	4.03	0.127	4.99	16.35	16.22
CtCls	7.14	5.14	0.135	6.46	19.02	18.9
Diff %	-22.11	-27.5	-6.3	-29.38	-16.33	-16.41

10B Females - Indexation from Haycock

	Mean	StDev	Minimum	Median	Maximum	Range
GFRs	5.48	3.7	0.01	4.73	15.44	15.44
CtCls	7.73	5.35	0.208	6.03	21.36	21.15
Diff %	**-41.12**	**-44.4**	-2211.1	-27.4	-38.3	-37.03

10B Females - Indexation from Lee						
	Mean	StDev	Minimum	Median	Maximum	Range
GFRs	5.85	4.03	0.127	4.99	16.35	16.22
CtCls	7.14	5.14	0.135	6.46	19.02	18.9
Diff %	-22.11	-27.49	-6.3	-29.38	-16.33	-16.41
10B Females - Indexation on Height						
	Mean	StDev	Minimum	Median	Maximum	Range
GFRs	4.12	2.82	0.04	4.24	10.03	9.98
CtCls	4.03	2.67	0.01	3.76	11.49	11.48
Diff %	***2.18***	***5.18***	76.19	11.34	-14.58	-14.96

The tables above show the statistical data of indexed GFRs from the Model and of CtCl/s/min, where some data on the percentage difference between data of GFRs from the Model and data of CtCls/min are stressed by bold characters or by bold and cursive characters. The data in bold only concern the differences in mean and standard deviations of the indexations on BSA by Haycock, whereas the second in bold and cursive characters are the same statistics of the indexations by height in males as well as in females. The emphasized data from the Haycock indexation show that the very relevant differences between the compared means and standard deviations of GFRs and CtCls/min were higher than 40% and were strongly different from the results with other indexations. This difference explains the significant difference in the Haycock indexation in tables 5 and 9, b versus b1. The data emphasized in bold and cursive are related to the indexations on height and similarly concern the percentage difference between the mean and standard deviation of GFRs versus those of CtCls/min, but in this case show a small difference, particularly for the mean.

The final step defines the relationship of the item dispersion between the GFRs from the Model and CtCls/min on the basis of three statistics suitable for appreciating the degree of dispersion of a variable, the coefficient of variation, the variance and the skewness.

The consistent data are reported in tables 11A and 11B. The data in bold stress the lowest value in the considered partition, and it is possible to see that there are partitions that share the lowest values.

The data of variance, skewness, and coefficients of variation of CtCls/min were regressed on the corresponding data of the decreased GFRs from the Model to define the degree of consistency in the items dispersion between the two compared variables. The results are reported in tables 12A and 12B and clearly show the high correspondence of the indicators of dispersion between the GFRs from the Model and the CtCl/min values.

11A - Males - statistics of the items dispersion of the variables			
Variables	Coeff var.	Variance	Skewness
CtCl/min	0.303	6.864	0.613
CtCl/min indexed DuBois	**0.275**	4.812	**0.439**
CtCl/min indexed Haycock	0.281	4.878	0.45
CtCl/min indexed Lee	**0.275**	4.621	**0.439**
CtCl/min indexed Height	0.282	**2.046**	0.559
Variables	Coeff var.	Variance	Skewness
Decreased GFR	**0.0906**	24.5	0.0426
Decreased GFR indexed Du Bois	0.111	37.9	0.223
Decreased GFR indexed Haycock	0.108	35.5	0.274
Decreased GFR indexed Lee	0.111	36.4	0.223
Decreased GFR indexed Height	0.103	**12.56**	**0.114**

11B - Females - statistics of the items dispersion of the variables			
Variables	Coeff	Variance	Skewnes
CtCl/min	0.283	5.212	0.129
CtCl/min indexed DuBois	0.262	3.535	-0.0147
CtCl/min indexed	**0.261**	3.408	**-0.013**
CtCl/min indexed Lee	0.262	3.394	-0.0147
CtCl/min indexed Height	0.276	**1.34**	0.058
Variables	Coeff	Variance	Skewnes
Decreased GFR	**0.0896**	24.62	0.145

Decreased GFR indexed	0.113	41.05	-0.059
Decreased GFR indexed	0.111	39.39	-0.035
Decreased GFR indexed	0.113	39.42	-0.059
Decreased GFR indexed	0.102	**11.4**	**0.034**

Tab. 12A - Males - Relationships among variance, skewness and coefficient of variation between the GFRs from the Model and CtCl/min				
Statistics of regressions				
predictor	responder	R	R^2	P
Variance of GFRs and indexations	Variance of CtCl/min and indexations	0.993	0.986	0.0072
Skewness of GFRs and indexations	Skewness of CtCl/min and indexations	0.96	0.933	0.009
Coeff. Var. of GFRs and indexations	Coeff. Var. of CtCl/min and indexations	0.983	0.966	0.0026

Tab. 12B - Females - Relationship of Variance, Skewness and Coefficient of variation between GFRS by Model and CtCl/min				
Statistics of regressions				
predictor	responder	R	R^2	P
Variance of GFRs and indexations	Variance of CtCl/min and indexations	0.999	0.999	0.000
Skewness of GFRs and indexations	Skewness of CtCl/min and indexations	0.992	0.985	0.0008
Coeff. Var. of GFRs and indexations	Coeff. Var. of CtCl/min and indexations	0.972	0.945	0.0055

IV. DISCUSSION AND CONCLUSIONS

Two fundamental comments have to be made about the results shown in all of the tables above. The first is that the only negative comparison between the data from the Model and the data on CtCl/min and its indexations was found only when comparing the differences a) between the residuals of the regression GFRs indexed by Haycock vs non-indexed GFRs and b) between the residuals of CtCls/min indexed by Haycock vs non-indexed CtCls/min in males and in females. These results were shown to be due to the very relevant differences between means and standard deviations of the two compared variables in this particular comparison, unlike that in all the other indexations. The second and more relevant observation was the different sample sizes for the compared variables, 100 male and female subjects for GFRs versus 45 males and 94 females for CtCl/min. This difference did not prevent the many significant relationships between the two variables, whose similarities were based only on measures of creatinine clearance. For a better understanding of the reason for these strong relationships, it is important to remember that the theoretical variable from the Model was not based on data randomly created but on likely real values [9]. Furthermore, the body surfaces on which the theoretical measured values were indexed were calculated using real somatic measures drawn by the Tables of Metropolitan Insurance 1983 [10]. Therefore, the indexed data from the Model had an adequate likelihood, which sufficiently explains the high correlation between the indexes of dispersion for the GFRs from the Model and CtCls/min. Taking into account the results of this study, and particularly the best result obtained from the indexed items vs non-indexed when using indexation on height, it seems to be quite reasonable to conclude that 1) the procedures followed in the Model for evaluating the effects of different indexations on item distribution can be used as a model to study the positive or negative effect of a new method or formula of indexation on the items distribution and that 2) this study further confirms that indexing on height produces the lowest variation in the measured values.

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