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Rederived Values of the Eight Coefficients of the Crohn's Disease Activity Index (CDAI)

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A previous paper reported derivation of the Crohn's Disease Activity Index (CDAI) from data on 112 patients. We have now rederived the values of the eight coefficients of the CDAI using data from 1058 visits of patients enrolled in the National Cooperative Crohn's Disease Study and the Trial of Adjunctive Sulfasalazine in Crohn's Disease. The rederived coefficients are similar to the original ones. New and original index values calculated on the same data from patient visits correlate very highly. Because there is so little difference between the original and the rederived versions, continued use of the original version is suggested in order to maintain comparability of new studies employing this tool with those previously accomplished.

Because the Crohn's Disease Activity Index has been integral to both the National Cooperative Crohn's Disease Study (NCCDS)[1] and the Trial of Adjunctive Sulfasalazine in Crohn's Disease (TAS-Study)[2] and has been adopted by other prospective trials as well,[3,4] it appeared worthwhile to obtain further data which might address the validity of the index per se during the course of these studies.

We previously published information on how the index was developed.[5] Essentially, data were prospectively collected from 187 visits on 112 patients with Crohn's disease. Information on 18 predictor variables was gathered at each visit, and in addition, the attending physician recorded his overall evaluation of the patient's clinical status. A multiple regression computer program with suppression of the constant factor and stepwise deletion of variables was used to develop the index. Each of the 18 variables was scaled so that a state of good health had a zero value, and increasing positive values were associated with increasing ill health. Through the process of variable deletion, the regression was narrowed down to the eight predictor variables listed in Table 1. The coefficients derived for the variables were then standardized to give the smallest of them a value equal to one, and then they were rounded to one significant digit. The resultant index satisfied the following requirements: (1) It incorporated factors which are important indicators of disease activity, (2) it utilized observations readily available at time of a patient's visit, (3) it considered only coefficients with intuitively appropriate sign, (4) it was simple to compute (see Appendix), (5) it demonstrated visit-to-visit changes consistent with overall appraisals, (6) it correlated well with overall appraisals of disease activity, and (7) it weighed components so as to optimize accuracy of predicting physician appraisals. Using data from 1058 patient-visits during the NCCDS and TAS studies, the coefficients of the eight variables of the CDAI have been rederived. These coefficients agree remarkably well with the original formula; the index using either set of coefficients predicts the physicians's global assessment of patient status with acceptable accuracy.

Methods

In rederiving the coefficients of the index, only the eight variables finally selected in the original index were examined, because data on most of the others were not regularly collected. These variables were scaled in the same manner as originally, and each item was coded according to the conventions of Table 1 for each patient visit. At each visit the clinicians caring for study patients were asked to record their overall evaluation of the patient's clinical status before calculation of the Crohn's Disease Activity Index. These included ratings of "very well," "fair to good," "poor," and "very poor," which were assigned respective numerical values of 1, 3, 5, and 7, as in

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Table 1. Independent Variables of the Crohn's Disease Activity Index

Variable	Item (and experience in original group of 112 patients)
x_1[a]	Liquid or very soft stools—number in 1 wk: (15%, none; 5%, 1-4; 18%, 5-9; 22%, 10-19; 28%, 20-49, and 12%, 50-98)
x_2	Abdominal pain—sum of 7 daily ratings: 0 = none, 1 = mild, 2 = moderate; and 3 = severe. (42%, zero; 19%, 1-4; 11%, 5-9; 24%, 10-19; 4%, 20-21)
x_3	General well-being—sum of 7 daily ratings: 0 = generally well; 1 = slightly below par, 2 = poor, 3 = very poor, 4 = terrible. (37%, 0; 17%, 1-4; 23%, 5-9; 18%, 10-19; 6%, 20-28)
x_4	Symptoms or findings presumed related to Crohn's disease: (1) Arthritis or arthralgia (2) Skin or mouth lesions, such as pyoderma gangrenosa or erythema nodosum (3) Iritis or uveitis (4) Anal fissure, fistula, or perirectal abscess (5) Other bowel-related fistula, such as enterovesical, etc. (6) Febrile episode exceeding 100°F during past week For each of these categories corresponding to patient's symptoms or findings add 1. (68%, no categories positive; 30%, 1; 9%, 2-3)
x_5	Taking Lomotil or opiates for diarrhea: 0 = no (71%), 1 = yes (29%)
x_6	Abdominal mass: 0 = absent (83%); 2 = questionable, sense of fullness or garden-hose type mass (4%); 5 = present (13%)
x_7	Hematocrit—(47 minus hematocrit), males; (42 minus hematocrit), females. (Figures are 48 and 43 for Denver and Albuquerque because of altitude.)
x_8	Body weight − 100 × (1 minus [body weight/standard weight]): (mean = 7.2%, standard deviation = 11.2%)

[a] Taken as one-third of actual value if an ileostomy was present.

the original study. Data on 1058 patient-visits were thus collected during the latter part of the NCCDS and throughout the TAS study.

The prototype of multiple regression is the equation:

$$y = b_0 + b_1x_1 + b_2x_2 + \ldots b_kx_k.$$

Standard computer programs permit computation of coefficients (b-values) from an array of collected data (x and y values) including an option to force a zero value to b_0. As noted previously,[5,6] suppression of b_0, when independent variables are coded (as here) with zero indicating good health and progressively positive values meaning increasing ill health, results in a composite "descriptive function" of disease. Coefficients from the 1058 patient-visits were computed with suppression of b_0, and the results are shown as the first column under "Validation Computations" of Table 2. In seeking a simple set of coefficients in the original study, we divided all coefficients by the smallest one, b_8, so that it would have a standardized coefficient of one. Standardized coefficients were then rounded to one significant figure. Because the original CDAI has now been used for several years, and particular numerical values of the index have acquired subjective meaning to clinicians familiar with it, we wished numerical values of the rederived index to be associated with the same general clinical interpretations as these values would have had under the old index. To accomplish this objective, the second step under "Validation Computations" in Table 2 differed from that of the original computations. A multiplication factor was computed as the mean CDAI (using the original index) for the 1058 visits divided by the corresponding mean of y-values, which were computed by using the values for each component of the index observed at the visit (x values) and the coefficients given in the first column under "Validation" in Table 2 (b-values) in the formula:

$$y = b_1x_1 + b_2x_2 + \ldots b_kx_k.$$

This factor, 61.1, was then multiplied by the individual coefficients to give the standardized value in the second column under "Validation." This step guaranteed an identical mean value for these data under the two formulas, and it is reasonable to expect that the dispersion of values will

Table 2. Comparison of Coefficients from Original and Validation Samples

Variable number	Variable	Original computations First visits on 112 patients			Validation computations 1058 patient visits		
		Coefficient	Standardized	Rounded	Coefficient	Standardized	Rounded
x_1	No. liquid/soft stools, 1 wk	0.0246	1.95	2	0.0371	2.27	2
x_2	Sum of 7 daily abdominal pain ratings	0.0648	5.14	5	0.0997	6.09	6
x_3	Sum of 7 daily ratings, well being	0.0907	7.29	7	0.0951	5.81	6
x_4	No. of other groups of symptoms/findings	0.2809	22.27	20	0.4331	26.46	30
x_5	Taking opiate antidiarrheal agent (1 = yes, 0 = no)	0.4516	35.80	30	0.0692	4.23	4
x_6	Abdominal mass (0 = no, 5 = yes)	0.1314	10.42	10	0.2147	13.12	10
x_7	Males: (47—hematocrit) Females: (42—hematocrit)	0.0798	6.33	6	0.0938	5.73	6
x_8	Body weight percent below standard wt.	0.0126	1.00	1	0.0042	.26	1

be similar. The last step was to round these values to one significant figure, as indicated in the last column of Table 2.

The means, standard deviations, and correlation coefficients between original and new formula CDAI's on the 1058 patient visits shown in Table 3 were calculated using standard methods.[7]

Results

The standardized, rounded coefficients for each of the eight items of the index derived from both the original and validation samples are presented in Table 2.

Table 3 gives the distribution of CDAI values as related to physicians' ratings of patient status. Several trends are apparent from this table:

1. Means and standard deviations of CDAI's by the two methods were very comparable when applied to the same patient-visits within physician rating groups. High correlations between indices for the two sets of coefficients were obtained within these groups.
2. Patients participating in the studies were not as sick as those from whom the CDAI was originally derived. This is evident from the mean CDAI's as well as by the distribution of physician ratings.
3. Physicians tended to assign unfavorable ratings in the face of lesser rises in CDAI for study patients than was the case for the original group. As a result, slightly more overlap of CDAI values is seen from one global rating to the next.
4. There is nevertheless still a clear relationship between physicians' overall appraisal and both the original and the newly derived indices.

Discussion

Using data on each item of the Index and the physician's global assessment of patient's clinical status, we have obtained coefficients for the eight items which are remarkably similar to those of the original version. We were not able to test for the 10 predictor variables deleted in the stepwise regression of the original study, therefore we cannot say that, had we done so, the same subset of eight predictors would have emerged. The taking of opiate antidiarrhea agents (x_5) and the patient's body weight (x_8) each appear less important components of the rederived version than of the original. The presence of other symptoms and findings is given slightly more weight in the new version. The close similarity of coefficients in the original and rederived indices gives confidence that the relative weighting of the eight components in the original index was appropriate. It should be noted that in deriving both the original and validation values of coefficients, one of the coefficients, that for body weight, was not statistically significantly different from zero. It was included nonetheless because it was considered clinically important by the investigators.

The patient population of the NCCDS and TAS studies may be compared with that from which the index was originally derived. The patients in the studies were less ill than those surveyed in derivation of the index. This is not surprising, because almost 50% of the patients in the NCCDS were in remission and entered that portion of the study which tested a prophylactic effect of the study medications. It is more difficult to explain the apparent increase in sensitivity of study physicians to alterations in patient status. Perhaps when physicians encountered patients in the context of the study they were more likely to rate a given degree of illness as being severe than they would have been in a nonstudy setting. This might merit further study as a phenomenon of physicians' clinical behavior. The CDAI offers a tool for such studies, because it does not depend upon subjective input from the evaluating physician apart from his judgement as to whether an abdominal mass is present.

When both original and rederived versions of the CDAI were applied to the same set of data from 1058 patient visits, the agreement in prediction of the physician's global assessment was extremely close, suggesting that there is little advantage in adopting the rederived coefficients in preference to the original set. The desirability of maintaining com-

Table 3. CDAI Values Compared with Physicians' Global Rating of Patient Status for Original and Study Patients

Physicians' rating	Original paper, original formula			Current data					
					Orig. formula		New formula		
	Number of units	Mean	SD	Number of units	Mean	SD	Mean	SD	Correlation coefficient
Very well	69	82.6	58.7	463	70.0	54.9	69.0	53.7	0.986
Fair to good	84	191.6	74.2	488	141.0	73.1	140.3	72.2	0.987
Poor	31	313.9	103.2	90	254.5	92.0	252.9	84.3	0.969
Very poor	3	517.0	—	17	321.0	100.2	314.5	95.8	0.994
Total	187	176.9	—	1,058	122.5	—	121.5	—	—

Table 4. Program for Computing CDAI Using TI-59 Calculator

Address at start of line	The program[a]	Use and explanation of the program[b]			
		User enters	User presses	Calculator does	Calculator displays
000	2nd LBL A STO O 1 × 2 = STO O O RCL O 1 R/S	x_1	A	$2 \times x_1$	x_1
012	STO O 1 × 5 = SUM O O RCL O 1 R/S	x_2	R/S	$+ 5 \times x_2$	x_2
022	STO O 1 × 7 = SUM O O RCL O 1 R/S	x_3	R/S	$+ 7 \times x_3$	x_3
032	STO O 1 × 2 O = SUM O O RCL O 1 R/S	x_4	R/S	$+ 20 \times x_4$	x_4
043	STO O 1 × 3 O = SUM O O RCL O 1 R/S	x_5	R/S	$+ 30 \times x_5$	x_5
054	STO O 1 × 1 O = SUM O O RCL O 1 R/S	x_6	R/S	$+ 10 \times x_6$	x_6
065	STO O1 x ⇆ t O 2nd x ≥ t O 8 1	Hematocrit[c]	R/S	(Skip to female formula if entry is negative)	—
072	4 7 − RCL O 1 = GTO O 8 7	—	—	(Male: $x_7 = 47 - Hct$; skip female)	—
081	4 2 + RCL O 1 =	—	—	(Female: $x_7 = 42 - Hct$)	—
087	× 6 = SUM O O RCL O 1 R/S	—	—	$+ 6 \times x_7$	Hematocrit
095	STO O 1 R/S	Weight	R/S	—	Weight
098	÷ RCL O 1 = 1/x × 1 O O + .5 = 2nd INT	Std. Wt.	R/S	(% Std = 100 × wt÷std)	—
112	± + 1 O O =	—	—	($x_8 = 100 - \%$ Std)	—
118	+ RCL O O = INV SBR	—	—	$+ x_8 =$ CDAI	CDAI
123	—	—	—	—	—

[a] Each program step as entered is separated from the next by a space. The calculator at times combines two input steps into one step in memory, which accounts for the discrepancies between number of spaces and addresses at start of lines. [b] A test example for a female patient is as follows: $x_1 = 28$, x_2 7, $x_3 = 14$, $x_4 = 1$, $x_5 = 0$, $x_6 = 2$, hematocrit = 40 (enter negative for female), body weight = 100 lbs., and standard weight = 150 lbs. The calculated CDAI should be 274. [c] Hematocrit is converted to a negative value (press ±) if this is a female patient.

parability with existing studies leads us to recommend continued use of the original coefficients in future clinical studies of Crohn's disease where the CDAI is used.

We have stated that the CDAI is simple to compute. Mee et al.[8] dispute this fact and propose that the erythrocyte sedimentation rate or C-reactive protein correlate about as well with a global rating of patient status. The use of a hand-held programmable calculator as outlined in the Appendix, should render computation less "cumbersome." The numbers which Mee et al. report would not give much power in comparing one index with another, and the global rating per se is of course fallible. A priori, our clinicians have more confidence in an index combining multiple variables previously considered pertinent than in a single laboratory measure which may be affected by irrelevant factors.

Appendix: Use of Hand-held Programmable Calculators to Compute the CDAI

Hand-held calculators with magnetic card program storage are now available at low cost. While paper-and-pencil computation of the index at a patient visit is easy, such a calculator makes it even easier.

Two popular calculators of this type are the Texas Instruments TI-59 and the Hewlett Packard HP-67. These and similar calculators may be readily programmed to perform these computations. Table 4 is a program for the TI-59. Once this is entered and tested, it may be permanently stored on a magnetic card. It is then readily reentered into the calculator whenever it is necessary to calculate a CDAI. We believe that the index is useful to clinicians and may find a place in the routine management of patients with Crohn's disease as well as in clinical trials such as these.

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