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METHOD OF STAGING SYSTEM CONSTRUCTION

by

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In a previous publication the purpose and concepts of constructing staging systems were presented (KUROHARA & GEORGE 1970). A 'split then lump' tabulation procedure was demonstrated to produce an 'optimal' staging system for carcinoma of the corpus uteri recurrent after total hysterectomy. Each level of stage was separated distinctly from each other.

In this paper the same procedure is used with slight modification to demonstrate construction of staging systems for primary adenocarcinoma of the corpus uteri.

Materials and Methods. In this approach to staging each of the variables or factors customarily known to represent measures of prognosis in a specific variety of carcinoma is discriminated into two or more levels according to survival rates or similar parameters. The population of patients is subdivided into groups, accounting for a combination of levels of each of the variables. Subsets of patients with similar survival rates are then combined into fewer categories with distinct differences in rates, depending on the clinical characteristics of the carcinoma process as well as on the sample size.

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Table 1

Anatomic sites of involvement according to prognosis. Possible sites or regions of involvement by adenocarcinoma originating in the corpus uteri, are indicated in columns two through six.

Primary corpus	Cervix	Upper vagina	Lower vagina	Pelvis	Bladder or rectum	Distant	Per cent		5-year survival*	
+	—	—	—	—	—	—	61	(725)	→ 61	(725)
+	+	—	—	—	—	—	37	(35)	→ 37	(35)
+	—	+	—	—	—	—	33	(3)	18	(11)
+	+	+	—	—	—	—	13	(8)		
+	—	—	+	—	—	—	0	(10)		
+	+	—	+	—	—	—	0	(2)		
+	—	+	+	—	—	—	0	(2)		
+	—	—	—	+	—	—	13	(15)		
+	+	—	—	+	—	—	0	(9)		
+	—	+	—	+	—	—	0	(1)		
+	+	+	—	+	—	—	0	(3)	4	(68)
+	—	—	—	+	—	—	0	(1)		
+	+	+	+	+	—	—	0	(2)		
+	—	—	—	—	+	—	0	(3)		
+	—	—	—	+	+	—	0	(1)		
+	+	—	—	+	+	—	0	(1)		
+						+	6	(18)		

+ Carcinoma present at site.

— Carcinoma not present.

For distant spread (last row) + or — are not specified for sites within pelvis.

* Crude 5-year rates are shown for groups of patients with various combinations of sites of involvement found in this series. Groups with small numbers of cases have been combined according to extent of spread and prognosis. Crude rate = number alive/number at risk expressed as percentage (number at risk).

The material consisted of 835 primary cases of adenocarcinoma of the corpus uteri with complete clinical and histopathologic information suitable for this investigation. The patients were seen at the Roswell Park Memorial Institute during 1940 through 1960. None of them was lost to follow-up for at least seven years after diagnosis.

Anatomic site of involvement, uterine cavity depth and uterine size were the three commonly used variables in staging of carcinoma of the corpus uteri. Histologic grade and age were also included, because they are the next most clinically sensible staging variables to be considered. Other variables were not examined because of the limited number of cases.

In order to show the probabilistic significance of the particularly constructed set of prognostic classes or stages, i.e. the chance occurrence of these staging systems is low, an algorithm was devised to perform the following operations:

1. Randomly permute and partition subsets of patients in a $4 \times 4 \times 2 \times 2$ array consisting of the respective age, histology, uterine size and uterine cavity depth variables as axes for lesions confined to the corpus (Table 1). Because of the small sample size the anatomic dimension was not incorporated into the array, i.e. each of the three extracorporeal subgroups, was not subdivided according to the above four variables but considered separately in later computations.

Two situations of random permutating and partitioning were considered. In the first situation, the subsets in the four dimensional intracorporeal array were grouped into stage subgroups without regard to their initial positions in the arrays. A programmed technique (IBM) was utilized to randomly permute the positions of these subsets, and to randomly partition them into subgroups consisting of anywhere from 2 to 22 subsets. This procedure could produce a maximum of 33 stage subgroups to a minimum of three. However, such extreme conditions of staging are unlikely to occur.

In the second situation, the positions of subsets of patients in the multidimensional array were considered to simulate somewhat in a random fashion the process by which the particular staging systems were constructed (Tables 3, 4). The array was subdivided into stage subgroups by starting at the origin and taking integer distances along each of the axes in order of variables with decreasing prognostic discrimination, i.e. in order of age, histology, uterine size and uterine cavity depth. The first stage group would be located closest to the origin. The next one was produced by continuing along axes in the same order, etc.

When the limits of any of the axes values, four for age and histology and two for uterine size and cavity depth, were reached, these axes were excluded in subsequent partitionings. The choice of integer distances to travel along each of the axes was done by the permutation program, using integers 0 up to 4. Staging subgroups consisting of less than two subset cells or those with no patients, were combined with the next subgroup in the process of partitionings.

2. Calculate the weighted averages of 5-year survival rates of subgroups of patients, representing those for stages obtained by the above procedures.

3. Combine the patients with uterine cervix involvement with those of stage subgroups with intracorporeal lesions associated with 5-year survival rates of less than 40 per cent.

4. Rank the rates from one to the highest integer of stages.

5. Calculate the Pearson's linear and Spearman's rank correlation coefficients, Wilcoxon rank-sum statistic (Bross 1954) for survival rates against stage ranks, and chi-square values (corrected for continuity) for differences between adjacent survival rates.

Several criteria for the evaluation of effectiveness of clinical stages were used and tested according to the following statistics: Pearson's and Spearman's correlation coefficients (R and Rs), Wilcoxon statistic (W), and each of them multiplied by the number of significantly different ($X^2 > 3.84$) adjacent survival rates plus one. The frequency distribution of each of these six statistics for 20 000 machine-constructed staging systems, was compared for the two situations. The Wilcoxon statistic times the number of stage levels with nonoverlapping rates (WND) appeared to be the best measure of effectiveness. For example, one set of rates, 37, 53, 62 and 73 per cent, and another 33, 45, 61 and 66 per cent (61 and 66 overlap) yielded W of 43 and 43, and R and Rs of 0.23 and 0.23, whereas WND's were 43×4 and 43×3, respectively.

Results

Table 1 shows groups of cases subcategorized according to anatomic sites of involvement of organs by carcinoma, listed in increasing order of advancement of disease. Carcinoma begins in the corpus (first column), spreads to cervix (second column), and then to upper vagina, lower vagina, pelvis, bladder, rectum or distant sites (column-wise, right and row-wise, down). For the six sites or regions to which carcinoma of the corpus uteri may spread, there were 64 possible combinations of involvement, however, only 17 of them actually occurred in this investigation. Cases with metastasis outside the true pelvis were considered in one group irrespective of involvement of carcinoma elsewhere in the pelvis.

The largest group consisted of patients with carcinoma confined to the organ of origin with a 5-year survival rate of 61 per cent. The proportion of such cases is large, indicating that this tumor does not have great propensity to spread early. The next largest group consisted of patients with carcinoma spread to cervix. The survival rate has dropped to roughly one-half that of the former. The number of cases for groups with combinations of more distant sites of spread is small with inconsistent and generally low rates close to zero. Because of this, such cases are combined into a group with upper vaginal involvement and into one with more extensive sites of spread. This arrangement yielded a maximal WND 'statistic' of 353. Thus, four prognostic levels of spread of corpus carcinoma are considered: corporeal, cervical, upper vaginal and more extensive.

Table 2

*Age, histology, uterine cavity depth or uterine size according to prognosis**

Variable	Level 1	Level 2	Level 3	Level 4	WND 'statistic'
Age (yrs)	< 50	50—59	60—69	> 70	
	73 (111)*	62 (203)	53 (328)	37 (197)	172
Histology	Adenoacanthoma Grade 0	Adenocarcinoma Grade I	Adenocarcinoma Grade II	Adenocarcinoma Grade III	
	66 (68)	61 (518)	45 (83)	33 (166)	129
Uterine size	*Normal*	*Large*	*Very large*		
	58 (350) |	53 (471)	33 (18)		8
Uterine cavity depth (cm)	$\leqslant 7$	8	9	$\geqslant 10$	
	55 (213)	54 (261)	59 (174) |	50 (191)	1

* Crude 5-year survival rate, per cent (number at risk).
Vertical line indicates cut-off points for conversion of uterine cavity depth and uterine size values into binary ones.

The prognostic gradient for levels of variables, age at diagnosis, histologic grades, uterine size and uterine cavity depth are given in Table 2. Five-year rates for age ranges, < 50, 50—59, 60—69 and $\geqslant 70$ years, are 73, 62, 53 and 37 per cent, respectively (WND $= 172$). Though this partitioning of patients into these age groups did not yield the maximum WND value of 180 as for another set, it was chosen for convenience. Rates for histologic grades, 0 to III, are 66, 61, 45 and 33 per cent, respectively (WND $= 129$). Those for uterine sizes, N, L and VL, are 58, 53 and 33 per cent (WND $= 8$), and for uterine cavity depths, $\leqslant 7$, 8, 9 and $\geqslant 10$ cm, are 55, 54, 59 and 50 per cent (WND $= 1$), respectively. Because the latter two variables are weakly discriminating of prognosis, they are demarcated into binary forms. For example, uterine sizes above normal values were associated with a crude 5-year rate of 52 per cent as compared to 58 per cent for those of normal size. Uterine cavity depths less than 10 cm were associated with a rate of 56 per cent as compared to 50 per cent for those 10 cm or more.

Table 3 shows in two dimensions the survival rates of 64 possible groups of patients with localized carcinoma according to age, histology, uterine cavity depth and uterine size. Because of the zero to small numbers of cases in some of the categories, the rates appear somewhat inconsistent. However, on close

Table 3

Combination of age, histology, uterine cavity depth and uterine size according to prognosis

Histology	Canal depth	Uterine size	Age (yrs)								Row totals	
			< 50		50—59		60—69		⩾ 70			
Adeno-acanthoma												
Grade 0	⩽ 9 cm	N	100	(7)*	63	(8)	79	(14)	60	(5)	76	(34)
		L	—	—	60	(5)	100	(6)	33	(3)	71	(14)
	> 9 cm	N	—	—	—	—	—	—	—	—	—	—
		L	50	(2)	75	(4)	75	(4)	—	—	70	(10)
Grade I	⩽ 9 cm	N	81	(21)	75	(59)	61	(77)	46	(46)	64	(203)
		L	88	(25)	62	(42)	69	(70)	38	(29)	61	(177)
	> 9 cm	N	—	—	—	—	67	(3)	50	(2)	60	(5)
		L	94	(18)	67	(24)	54	(33)	62	(21)	67	(96)
Grade II	⩽ 9 cm	N	67	(3)	78	(9)	70	(10)	38	(13)	60	(35)
		L	60	(5)	50	(4)	67	(6)	33	(6)	52	(21)
	> 9 cm	N	—	—	—	—	—	—	0	(1)	0	(1)
		L	—	—	100	(1)	14	(7)	40	(5)	31	(13)
Grade III	⩽ 9 cm	N	50	(4)	33	(3)	48	(15)	46	(13)	46	(35)
		L	75	(8)	73	(11)	46	(22)	15	(13)	48	(54)
	> 9 cm	N	—	—	—	—	—	—	—	—	—	—
		L	60	(5)	50	(6)	25	(16)	29	(7)	35	(34)
Column totals			81	(98)	68	(176)	59	(283)	42	(164)	60	(721)

* Crude 5-year survival rate, per cent (number at risk).

scrutiny, there are similarities in patterns of survival rates which have been lumped together. Some clinical judgment was used in lumping in order not to cross over excessively between levels of variables to cause confusion of clinical oncologic terms.

The composite tabulation for initial staging definition of corpus carcinoma is given in Table 4. In early lesions young patients (< 50 years) with low grade carcinoma (0 or I) do exceedingly well. Middle-aged patients (50—69) with grade 0 carcinoma also do well, but somewhat less than the above. Middle-aged patients with grade I carcinoma do well but not as well as the above two. Elderly patients (⩾ 70) with low grade lesions have a moderate degree of

Table 4

Composite tabulation of stages for corpus adenocarcinoma

Histology or anatomic site		Age (yrs)								
		< 50			50—69			⩾ 70		
Grade 0					IB	76	(41)			
		IA	88	(73)*				IIIB	47	(106)
Grade I					II	65	(308)			
	Cavity Depth									
Grade II or III	⩽ 9 cm		IIIA	59 (100)				IVC	33	(58)
	> 9 cm		IVB	34 (35)						
Cervix involved					IVA	37	(35)			
Upper vagina involved					VA	18	(11)			
More extensive spread					VB	4	(68)			

* Crude 5-year survival rate, per cent (number at risk).
Stages IVA, IVB, IVC are combined to give a 5-year rate of 34 per cent for 128 cases.

prognosis. In high grade lesions these patients do worse. Patients less than 70 years of age with high grade carcinoma (II or III) do fairly well when the uterine cavity measures 9 cm or less, and poorly when it measures over 9 cm. Elderly patients (⩾ 70) with high grade carcinoma also do poorly. Uterine size had the same effect as cavity depth.

In lesions not confined to the corpus only the anatomic sites of involvement are used in the definition of stages. When carcinoma has extended beyond the corpus down into the cervix survival is poor. It is even poorer when the tumour involves the upper vagina. Beyond the above anatomic confines, prognosis is close to nil.

Fig. 1 indicates the survival curves up through five years post-diagnosis for stages IA through VB (8 levels) as defined in Table 4. Considering the limitations

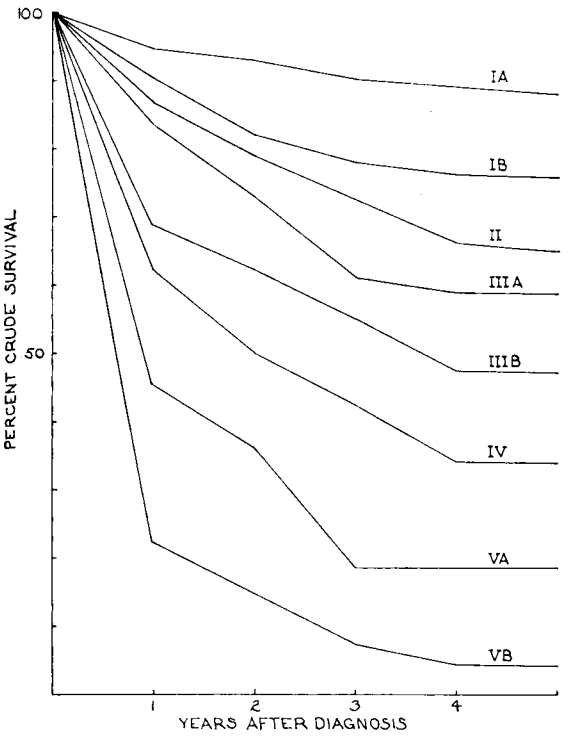

Fig. 1. Survival curves for clinical stages IA through VB.

of sample size, the curves are fairly well separated from each other without any crossing over. However, none of the adjacent 5-year rates were significantly separable from each other. The WND value and the Wilcoxon statistic were the same, 139.

Fig. 2 shows a plot of survival rates against midpoint of percentage cumulative incidence of stage levels. Because of the overlap between the rates for adjacent stages IA through VB, the alphabetized ones have been combined. Stages I, II, III, IV and V revealed no statistical overlap in rates at $p < 0.025$ with a WND value of 650. A theoretical curvilinear off-diagonal line which defines a segment of a circle, divides the total sample population space for staging into areas of patients alive beyond five years after diagnosis and dead before. The patients alive make up 54 per cent of the entire series and those dead 46 per cent. As suggested in a previous publication (KUROHARA & GEORGE 1970), an ideal staging system should approximate this line and, in addition, produce an even distribution of stages. The actual line fairly well approximates this ideal line, however, it deviates somewhat in the high region near stages I and II. One

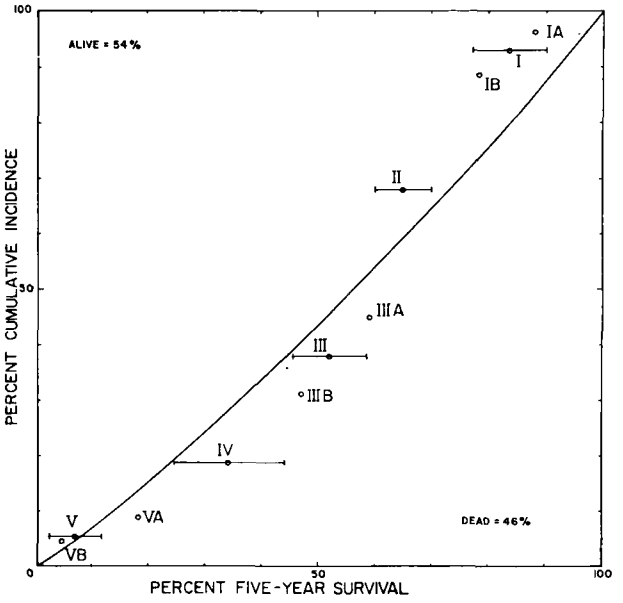

Fig. 2. Assessment of constructed staging system in primary adenocarcinoma of the corpus uteri. Horizontal bars denote ± 2 SE.

reason for this deviation is that stage II consists of a relatively large group of patients, 50—69 years of age with grade I lesions. If it were possible to separate this group further prognostically with the five variables employed, the actual curve would have been closer to the ideal. Another reason is low incidence of lesions spread outside the corpus. A larger proportion of stage V patients would push the plot of the stage IV group upward into the ideal line. Extracorporeal lesions made up only 14 per cent of this series rather than near 25 per cent in other series.

Thus, this procedure yields five prognostically distinct stages defined in the investigation of this case material:

Stage I: Carcinoma confined to corpus in patients less than 50 years of age with grade 0 or I lesions, or in patients 50 to 69 years with grade 0 lesions.

Stage II: Carcinoma confined to corpus in patients 50 to 69 years of age with grade I lesions.

Stage III: Carcinoma confined to corpus in patients less than 70 years of age with grade II or III lesions and with uterine cavity depth 9 cm or less, or in patients 70 years or older with grade 0 or I lesions. Tumor involves the cervix but not beyond.

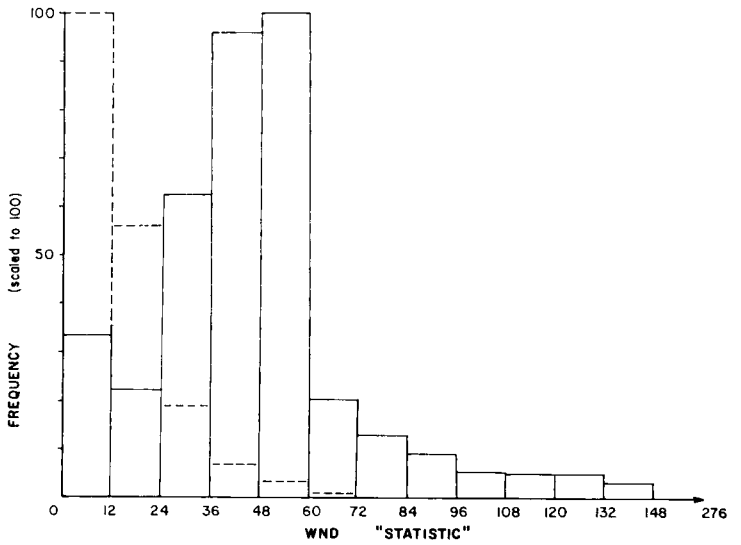

Fig. 3. Frequency distribution of WND 'statistic'. Solid line for adjacent position and dotted line for independent position situations.

Stage IV: Carcinoma confined to corpus in patients less than 70 years of age with grade II or III lesions and with uterine cavity depth greater than 9 cm, or in patients 70 years or older with grade II or III lesions.

Stage V: Carcinoma extending beyond the corpus and cervix.

It should be mentioned here that the above definitions of five clinical stages for adenocarcinoma of the corpus uteri, are only adaptable to this series of cases, and are not meant to be applicable to others. Generally, applicable staging systems can only be developed from a large number of cases of widely representative data.

Fig. 3 indicates the frequency distribution of the WND 'statistic' for 20 000 machine-constructed staging systems produced by random partitioning for each of the two probabilistic situations, when subgroup stages of patients according to age, histology, uterine cavity depth and size were considered independently of position and dependently on adjacent positions in the four-dimensional matrix. It is seen that the histogram of the former falls rapidly in an exponential manner from maximal frequency of 0 to 12 WND values to near zero at 60 to 72, the largest value being 156. In the latter there is a peaking of high values between 48 to 60, meaning that consideration of adjacent subgroup stages of patients

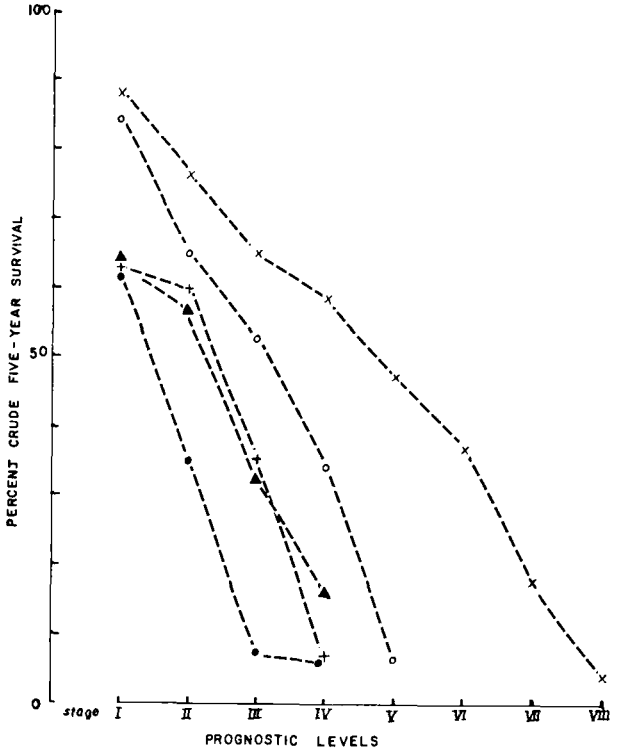

Fig. 4. Five-year survival rates against stage levels for several staging systems. O system A (WND 650), × system B (WND 139), ● International Staging System (WND 351), ▲ GUSBERG (WND 288), + HIRABAYASHI (WND 105).

has a better chance of generating more efficient staging systems. The highest WND value was 276. The distributions of the correlation and Wilcoxon chi-square values were close to normal, however being somewhat skewed toward the left for the latter.

Fig. 4 gives the plots of survival rates against one up to eight stage levels for several staging systems as applied to this sample population. The two optimal systems constructed for this series, indicated by plots 0 and X, have the highest W and Rs values, however, the one with less number of stage levels has a higer WND 'statistic' because each level was prognostically distinct from the next ($p < 0.025$). The International Staging System (KOTTMEIER 1963) has a relatively high WND value of 351, but there is essentially no difference in survival rates of stages III and IV. Systems proposed by GRAHAM & HIRABAYASHI (1968) and by GUSBERG (1966) had relatively low WND values of 105 and 288, respectively.

Table 5

Results of radiation therapy in adenocarcinoma confined to corpus according to stages

Clinical stage	Treatment groups*		
	Radiation	Surgery	Preoperative
I	88 (25)**	71 (17)	85 (72)
II	47 (88)	64 (55)	76 (165)
III	40 (89)	46 (37)	70 (80)
IV***	21 (41)	33 (9)	44 (43)

* Treatment groups consists of patients treated with irradiation alone, with total hysterectomy with or without postoperative irradiation, or with preoperative irradiation and total hysterectomy.
** Crude 5-year survival rate, per cent (number at risk).
*** Consists of cases with substage lesions IVB and IVC.

Table 5 demonstrates the applicability of this or similarly constructed staging systems for the comparison of treatment methods according to 5-year crude survival rates. Patients with stage I lesions respond equally well to each of these treatment methods. In stage II lesions, the result of the preoperative radiation therapy is best, that of the irradiation group is the worst, and that of the surgical group is intermediate. With advancing stage the results of all treatment procedures fall, and the differences between them decrease. In stages III and IV radiation therapy before total hysterectomy yield better results than radiation therapy alone or total hysterectomy alone. The results of the latter two treatment methods are similar. The data have been analyzed, in detail, according to incidence of carcinoma deaths, of local recurrence rates and techniques of irradiation. These specific results are not included and will be published elsewhere.

Discussion

A good system of clinical carcinoma staging should group patients with clinically similar tumor, as well as, host characteristics into distinct prognostic groups for the provision of comparing different methods of treatment. The reason for this is that the make-up of patients govern, to a large part, the end results of treatments of carcinoma.

For the construction of an optimal system of stages or of prognostic classes, knowledge of the survival characteristics of terms or of patient variables used in their definitions, is necessary. Without such knowledge, there is the danger

of mixing terms or variables with different degrees of prognostic distinctions when combining them into the various levels of stages.

Survival characteristics in carcinoma have been, in decreasing order of usage, the crude 5-year rates, corrected or adjusted five year rates (for age, causes of death, etc.), crude or corrected survival curves up to five or more years post-diagnosis or treatment depending on the follow-up duration, and slopes or some other parameter of survival curve functions. The crude 5-year rate was employed in this investigation because of its simplicity and relatively short duration of follow-up, and because most of carcinoma deaths occurred within five years of diagnosis. Five-year rates corrected for deaths due to other causes yielded essentially the same results. More complicated characteristics, such as survival curve slopes or functions were not possible to obtain from the limited sample population data.

In staging of corpus carcinoma the patient variables have been most often anatomic sites of involvement, less often uterine cavity depth or uterine size, and least often histologic grade. Anatomic sites of involvement have been generally accepted to be a valid concept of measurement of growth and spread for the many types of carcinoma causing the eventual death of patients. Degrees of spread of carcinoma from its site of origin have been found to predict prognosis well, provided that they have been defined optimally.

Levels of spread of carcinoma have generally been described as follows: (1) tumor confined to organ of origin, (2) tumor spread limited to adjacent tissues or organs, e.g. to upper vagina or paracervical tissues in gynecologic carcinomas, (3) tumor spread extensively to surrounding regions, e.g. to pelvic wall or lower vagina, and (4) tumor spread to distant sites, e.g. outside the true pelvis. The degrees of spread of corpus carcinoma is somewhat similar to the above. Although further refinement in degrees of anatomic sites of involvement was attempted, this was not found possible in this series of corpus carcinoma, since a great majority of cases (86 per cent) had disease in its earliest stage of spread, leaving only a small number for such subdivisions. Of the initially defined 16 levels of spread outside the corpus uteri, the latter 14 more extensive ones were combined. Thus, this variable was assigned only four convenient and realistic degrees of spread of carcinoma with maximal prognostic distinction.

Since corpus carcinoma tends to remain confined within its organ of origin, some authors have incorporated uterine cavity depth or uterine size to describe the prognostic behavior of cases withe localized disease (HIRABAYASHI & GRAHAM 1968). In this investigation these variables were found to be well correlated with each other and weakly discriminative, being applicable only for high grade lesions. Because of greater reliability in measurement, uterine cavity depth was employed rather than uterine size. A point of demarcations

between 9 and 10 cm was used to denote small and large uterine cavity associated with tumor size, because the number of cases with depths of 11 cm or more was too small.

Having employed all available clinical variables conceptualizing tumor spread and size, the next most sensible variable for staging would be histologic grade, as has been suggested elsewhere (GUSBERG 1966). In this investigation this variable was found to be more powerful in discriminating prognosis than uterine cavity depth or uterine size.

Age was added as an additional variable because of its relatively strong effect on survival (second to anatomic site). Although survival is expected to fall with age because of increased incidence of other age-dependent diseases, for some unknown reason it was still possible to discriminate rates between histologic grades even at advanced ages. That is, prognosis of elderly patients ($\geqslant$ 70 years) with low grade lesions (0 or I) were better than those with high grade lesions (II or III).

In order to segregate the large group of patients with carcinoma confined to the corpus, age, histologic grade and uterine cavity depth were employed in combinations. Seven levels of stages were identified for patients with carcinoma confined to the corpus (IA, IB II, IIIA, IIIB, IVB and IVC). These stages were combined with those spread outside the corpus to yield eight levels of stages for the total series. However, because of limitations in sample sizes, only five prognostically distinct levels of stages were possible.

Non-parametric statistical procedures were employed to show the degree of correlation between stage ranks and ranked proportion of cases survived. Both the Spearman rank correlation and the Wilcoxon rank-sum statistic indicated similarly the degrees of monotonic increase in survival rates with stage levels. Pearson's coefficient was usually the same as Spearman's, but because of uncertainty of normality of data the former was not relied upon. Since prognostic distinctions were not accounted for effectively by the correlation coefficients or by the Wilcoxon statistic, this aspect was incorporated by use of the chi-square test to distinguish overlap between survival rates of adjacent stages. The Wilcoxon statistic multiplied by the number of prognostically distinct stage groups, was found to produce maximal separation between the randomly constructed systems and those constructed by selection of patient characteristics. However, this single WND measure is not completely to be relied upon since its large value does not always guarantee good separation of all classes from each other. It is necessary to inspect the number of distinct groups, and sometimes the actual graphic plotting of stage levels against survival rates for certain high values obtained. This situation occurred in assessing the International Staging System which yielded a high WND value despite disproportionate

distribution of cases in stage I and poor distiction between stages III and IV.

Although it may argued that this procedure of constructing staging systems is not completely objective, and a more mathematical or statistical one should be employed, as of the time of this writing there seemed to have been no good solution. For this purpose, a randomization pseudo-permutative technique was employed to show that there would be less than five per cent chance of mechanically producing an equally good staging system. Of 20 000 systems generated, none had a WND 'statistic' and case distribution better than the one constructed.

It should be stated here that problems of grouping individuals into logical subsets have been previously encountered in the field of biology, psychology, anthropology and other related sciences. Approaches undertaken in attempt to solve specific problems in these areas, have been generally categorized as: frequency curve resolution, factor analysis and hierarchial clustering, based upon distance measures (JONES 1968). Names of some of the various methods using these approaches are: discriminant classification, Q and R factor analysis, common factor analysis, multiple factor analysis, numerical taxonometrics, taxonomic optimization, pattern analysis, similarity analysis, dissimilarity analysis, profile analysis, agreement analysis, etc.

Although several of the above statistical methods were employed in attempt to construct staging systems, they did not yield results statisfactory to us. Some of the reasons for their inapplicability were as follows: (1) linguistic differences in approach to this problem, (2) theoretical assumptions of properties of data, incompatible with facts, (3) requirement of parametricity of data and variable relationships, and (4) indeterminacy in functional relationship between variables, in loadings, in axis rotations, in distance measures, in similarity coefficients, etc., without previous information on group membership.

The suboptimal performance of currently proposed staging systems tested on this sample data, was due to the use of too few clinical staging information for purposes of simplicity, or due to the use of additional appropriate anatomic or histologic information but in combinations inefficient, to effectively discriminate prognosis in unselected series having a sizable proportion of elderly patients at high risk to other causes of death.

The International System of Staging employs only anatomic extent of spread for classification. Although simple, this system lumps a disproportionality large number of patients into the first category of stage (roughly 75 per cent in most series). The results of this investigation have demonstrated that patients with lesions still confined to the corpus may be still subdivided into smaller groups having 5-year survival rates ranging from 88 per cent down to 33 per cent. With such heterogeneity of patients grouped within one stage level, comparison

of treatment methods becomes unreliable without the necessity of strict statistical control which would also require a larger number of patients than required for a relatively more homogeneous subpopulation.

To decrease this extreme variation in patient types for lesions localized to corpus, other authors suggested employing uterine cavity depth or uterine size measurements with or without histologic grade to overcome this heterogeneity. HIRABAYASHI & GRAHAM (1968) employed uterine cavity depth of 8.5 cm to segregate these cases. However, they excluded cases dying of other causes, and in this way their staging system would be applicable only to patients whose death from carcinoma could possibly be predicted. Though this worked out well in these selected cases, its performance was poor in all cases with localized disease in this investigation.

GUSBERG (1966) divided intracorporeal lesions into these groups: cases with low grade carcinoma in normal sized uterus, those with low grade carcinoma in moderate sized uterus or with high grade carcinoma in normal sized uterus, and those with more advanced degrees of combinations of histologic grade and uterine size. His system yielded a relatively high WND value, however without prognostic distinction between stages I and II groups.

The production of prognostically distinct stages has the importance of minimizing variations in survival rates so that results of different treatment methods for patients within stage groups can be assessed reliably. The use of a poorly constructed staging system permits the physician under usual circumstances to select patients for each of the treatment methods so that the end results are governed by inhomogeneities in prognostically powerful variables rather than the treatment procedures themselves. As has been demonstrated in this investigation, as well as by others (GUSBERG 1966, NOLAN et coll. 1967), different treatment methods may be selected for different classes of patients based on histologic grade and uterine size. Hence, towards this end it is necessary to construct efficient staging systems with minimal heterogeneity in powerful biologic prognostic variables within each of the stage groups, with whatever applicable objective procedures available.

Finally, it should be stated that staging systems so assessed to be effective by this or any other quantitative measure available or yet to be developed, should ultimately be judged realistic by experienced clinicians and be compatible with current concepts in clinical oncology. It is believed that if this approach or any other similar one had been utilized previously, much of the numerous ineffective and incompatible staging systems would not have been proposed, and many man-hours would not have been wasted in utilizing such staging systems for the purpose of reporting and assessing end results of carcinoma treatment.

SUMMARY

The controversial subject of logical approaches to constructing 'effective' staging systems in carcinoma was presented. As an example, a simple but perhaps arbitrary 'split-lump' tabulation procedure was applied to the construction of an 'effective' staging system for a series of 835 primary cases of adenocarcinoma of the corpus uteri. The five particular clinical stages constructed by this procedure were prognostically distinct and directly related to crude five-year survival rates. It was demonstrated that this staging system was highly efficient relative to those currently proposed, and could not have occurred by chance. A generally acceptable system of staging for this type of carcinoma can only be developed by this or other similar methods with a much larger sample of patient data representative of many regions of the world.

ZUSAMMENFASSUNG

Die kontroversielle Frage logischer Ansätze, 'effektive' Stadien-Systeme für Karzinome zu konstruieren, wurde dargestellt. Als Beispiel wurde ein einfaches aber vielleicht willkürliches 'split-lump' Tabulationsverfahren verwendet, um ein 'effektives' Stadien-System für eine Reihe von 835 Primärfällen von Adenokarzinomen des Corpus uteri zu konstruieren. Die fünf besonderen klinischen Stadien, die durch dieses Verfahren konstruiert wurden, waren prognostisch distinkt und standen in direktem Verhältnis zur groben Fünfjahres-Überlebensrate. Es wurde nachgewiesen, dass dieses Stadien-System im Verhältnis zu den bisher verwendeten sehr effektiv ist und nicht zufällig entstanden sein kann. Ein allgemein anerkanntes System der Stadieneinteilung dieses Typus von Karzinom kann nur mit dieser oder anderen ähnlichen Methoden an einer wesentlich grösseren Gruppe von Patientdaten, die repräsentativ für viele Gebiete der Welt sind, entwickelt werden.

RÉSUMÉ

Les auteurs presentent le problème controversé que constitute la façon logique d'aborder l'élaboration d'un système 'efficace' de classement des stades du cancer. Comme exemple ils ont appliqué une méthode simple mais peut-être arbitraire à la construction d'un système de classement en stades 'efficace' pour une série de 835 cas primaires d'adénocarcinome du corps de l'utérus. Les cinq stades cliniques particuliers définis par cette méthode ont eu un pronostic différent et directement en rapport avec le taux brut de survie à cinq ans. Il a été démontré que ce classement par stade est très efficace par rapport à ceux qui sont habituellement proposés; ceci ne peut pas être dû au hasard. Seule cette méthode ou des méthodes similaires appliquées à un beaucoup plus grand nombre de cas provenant de nombreuses régions du monde pourront aboutir à un système de classement en stades qui puisse être accepté de façon générale pour ce type de cancer.

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