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INVASIVE SQUAMOUS CELL CARCINOMA OF THE UTERINE CERVIX

VIII. Survival and malignancy grading in patients treated by irradiation in Lund 1969–1970

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Abstract

The correlation between certain prognostic factors and the 10-year survival/lethality rate was analysed in 168 patients with invasive squamous cell carcinoma of the uterine cervix stage I A–II B treated by radiation therapy from 1969 through 1970. These factors included a malignancy grading system (MGS) consisting of 8 items: structure (P1), differentiation into cell type (P2), nuclear polymorphism (P3), mitosis (P4), mode of invasion (P5), stage of invasion (P6), vascular invasion (P7), and host-cellular response (P8). Histologic differentiation (1) and differentiation into cell type (11), the patient's age, the year of admission, the clinical stage (FIGO), and irradiation were also analysed. Many of these factors were correlated to the prognosis. However, the MGS system was superior as a predictive factor. Patients with a low MGS score had an extremely good survival rate at both the 5- and 10-year controls. The patients with a high MGS score had approximately 55 per cent lethality at 10 years. The MGS was significantly superior to each separate item as well as to each predictive factor ($p<0.05$). Further, no other important predictive factor could be identified after the MGS had been included in the multivariate analyses.

A multifactorial histopathologic malignancy grading system (MGS) in patients with invasive squamous cell carcinoma of the uterine cervix has been shown to have prognostic value in earlier reports (13–15).

The aim of the present investigation was to correlate various predictive factors to the long term prognosis for patients with invasive squamous cell carcinoma of the uterine cervix stage I A–II B treated by irradiation at the Gynecologic Section of the Department of Oncology, University Hospital, Lund, from 1969 through 1970. The MGS, histologic classifications, and clinical data were analysed in detail with respect to the 10-year survival/lethality rate.

Material

The material consisted of 208 patients with invasive squamous cell carcinoma of the uterine cervix in FIGO (3) stages I A to II B treated during 1969 and 1970. The boundary between stage I A and I B in cases where cone biopsy was performed was established according to the method of FRICK et coll. (4). Twelve patients advanced from stage I A to I B after the histopathologic reclassification.

Ten patients who had received less than 60 per cent of the intended radiation dose in point A (6) were excluded. No attention was otherwise paid to the tumour dose. Patients who exclusively received external irradiation were included. Thus, the material was reduced to 198 patients.

During the retrospective histopathologic malignancy grading, 30 patients were rejected because of

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Table 1

Dead, excluded and living patients (n=168)

MGS	Death from disease		Excluded due to intercurrent disease		Alive at 10-year follow-up	Total
	0–5 years	5–10 years	0–5 years	5–10 years		
≤12 p	0	0	1	4	33	38
13–15 p	4	5	6	2	79	96
≥16 p	16	2	2	0	14	34
Total	20	7	9	6	126	168

difficulty in evaluating some of the histologic parameters or because of poor quality of the biopsy, thus leaving 168 patients for the investigation.

Correction was made for patients who died from intercurrent disease within 5 years after onset of the disease (9 patients; n = 159). The duration of the follow-up was 10 years. The mean age at admission was 49 years. The stage distribution in the remaining 159 patients was: 23 in stage I A, 58 in stage I B, 53 in stage II A, and 25 in stage II B.

Methods

Pathology. All biopsies were originally classified according to the ACKERMAN & DEL REGATO scheme (1), into highly differentiated, moderately differentiated, and anaplastic carcinoma. A certain number of cases remained 'unclassified' in the primary report.

The cell type sub-classification of the tumours into large cell non-keratinizing, large cell keratinizing, and small cell carcinoma, suggested by REAGAN & WENTZ (11), was also used.

In all cases the pathologic reclassification with the malignancy grading system was performed on the pretreatment biopsies without knowledge of clinical stages, treatment, or the further course of the disease. The tumour cell population and the tumour–host relationship were considered separately. The evaluation of the tumour cell population was based upon the grading of tumour structure (P1), cell differentiation (P2), nuclear polymorphism (P3), and frequency of mitotic figures (P4) on a scale of 1 to 3. The tumour–host relationship was graded on a similar scale, by evaluation of the mode (P5) and the stage of invasion (P6), vascular invasion (P7) and the degree of lymphoplasmocytic infiltration (P8). These eight morphologic parameters constituted the MGS, which could thus range from 8 to 24 points (13, 15, 16).

Treatment. The patients were treated according to a modified 'Stockholm method' (6, 8). Early stage I A patients were given only two intracavitary treatments three weeks apart with a calculated dose in point A of 55 Gy. Patients with advanced stage I A, or stage I B and II B, were given primary external irradiation to the true pelvis without central shielding, using ^{60}Co or 33 MV photons. The absorbed dose in the true pelvis was 33 Gy ± 10 per cent given in 17 to 18 fractions and 44 Gy ± 10 per cent in 23 to 24 fractions for stages I B and II, respectively, using two opposing fields; one fraction a day, 5 fractions a week. Intracavitary treatment of the primary tumour was given three weeks after completion of external irradiation (7). The calculated dose in point A was 25 to 35 Gy. In cases with anatomic difficulties due to lack of satisfactory applicators, only external treatment was given. The calculated absorbed dose in the primary tumour was 64 Gy ± 3 per cent. The fourfield technique was used with two thirds of the absorbed dose given in a first series followed by an intermission of 2 to 3 weeks. The mean delivered total absorbed dose in point A (n = 198 patients) varied from 50 to 65 Gy, depending on the stages.

Statistics. A significance analysis was made for each factor in order to investigate significant correlation to the 10-year survival (χ^2-test or Fisher's exact test).

For estimation and significance testing in the regression analyses, program BMDP2R was used for the linear regression stepwise analysis, BMDPLR for the logistic regression analysis, and program BMDP2L (2) for the Cox regression. The latter was

Table 2

Ten-year survival/lethality (S/L) rates in stages I A to II B (n=159)

Stage	Survival rate (per cent)	No. of patients
I A	100	23
I B	88	58
II A	77	53
II B	68	25

Table 3

Age. Ten-year survival rates in per cent in various age classes (n=159)

Age at diagnosis (years)	Per cent	No. of patients
20–39	89	35
40–49	81	48
50–59	83	47
60–	79	29

Table 4

Histologic classification according to ACKERMAN & DEL REGATO (1)

Histologic differentiation	10-year survival	
	Per cent	No. of patients
High	97	32
Moderate	82	49
Anaplastic	72	47
Unclassified	87	31

performed in order to smooth the relation between survival rate and MGS.

An AID (automatic interaction detector) analysis, according to the OSIRIS package (9, 10) was performed. A mass significance analysis according to GAVATIN & EKLUND (5) was also performed. The reducibility criterion in the AID analysis was specified as 0.4 and the minimum number of observations was 10. All the variables analysed, except for classification according to ACKERMAN & DEL REGATO (1) and into cell type (11), were monotone. The classification according to the former authors was included as a free variable, because there were many unclassified cases in the primary histopathologic reports.

Survival curves according to KAPLAN & MEIER were carried out according to BMDP1L (2). Standard errors and confidence intervals were used as they were presented in the respective programs. Significance analyses of differences between correlation coefficients were performed as in the report by STENDAHL et coll. (14).

Results

Intercurrent deaths. The 10-year S/L rate for 168 patients who could be classified with the MGS is shown in Table 1. Fifteen women died from intercurrent disease during the 10-year period. The expected lethality according to the life table for the period 1971 to 1975 in Sweden was 16.6 (12), which agreed rather well with the number of cases who died intercurrently (n = 15). If the increased lethality due to the malignant disease (27 cases in the 10-year period) was considered, the expected number of deaths decreased to 15.5

Ten-year survival/lethality for different factors. The 10-year S/L rate for 159 patients in stage I A to II B is shown in Table 2. The 10-year survival rate was lower in stage II B than in stage I A + I B ($p<0.01$). Further, the difference between II A and I A was significant ($p<0.05$).

Table 3 shows the age distribution and the 10-year survival rates in different age groups. No significant difference existed between age groups with respect to the 10-year survival.

Table 4 illustrates the 10-year survival for the histologic classification according to ACKERMAN & DEL REGATO (1) in the primary histopathologic report. The highly differentiated carcinomas showed a better 10-year prognosis than the anaplastic ones ($p<0.01$).

For differentiation into cell type (11) the survival rate was 82 per cent (n=29) in large cell non-keratinized carcinoma, 84 per cent (n=123) in large cell keratinized carcinoma, and 43 per cent (n=7) in small cell carcinomas. The group of small cell carcinomas was too small for a conclusive prognostic comparison.

The S/L rate showed no significant differences related to the year of admission.

The number of lethal cases in the various MGS groups at the 5- and 10-year follow-up is shown in Table 1. The survival rates are presented in survival curves according to KAPLAN & MEIER (Fig. 1). The material is divided, in Table 1 and Fig. 1, into three categories:

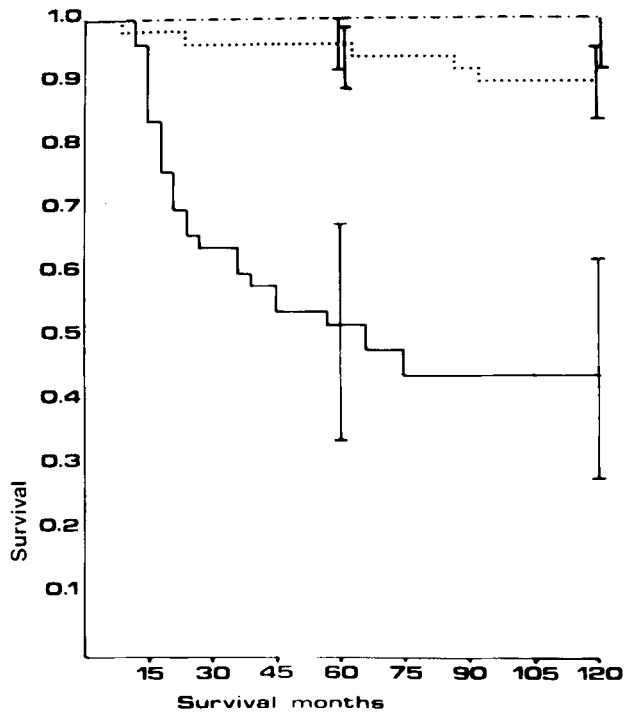


Fig. 1. Survival curves for 3 MGS classes (8–24 p). The 95% confidence interval for the 5- and 10-year survival. ≤12 p (n=38 - - -), 13–15 p (n=96 · · ·), >16 p (n=34 ——).

1) Low point MGS score patients (≤12 p) who all (100%) survived the 10-year follow-up, 95% confidence interval (94–100%).

2) A middle group of 13 to 15 points with 90 per cent survival at the 10-year follow-up, confidence interval (84–96%).

3) High point MGS score patients (≥16 p) with 45 per cent survival at the 10-year follow-up, confidence interval (28–62%). The 95% confidence intervals at the 5- and 10-year follow-up are given in Fig. 1.

The patients with the high point MGS score showed a significantly lower ($p<0.001$) survival than the two other groups at both the 5- and 10-year follow-up. A significant difference existed between the high point score group and the low point score group. Particularly remarkable was the low lethality risk in the patients with the low MGS point score. The lower confidence limit was 91 per cent survival at 10 years.

In Table 5, the distribution of patients and of survivors at the 5- and 10-year follow-up is shown with respect to MGS points. From the table it is possible to see the difference between the two follow-ups. It is evident that the lethality was higher during the first 5 years than during the second 5 years. Further, it is striking that the survival rate was higher among patients with a lower MGS score. This was true for both the 5- and 10-year follow-up. The MGS results in relation to the 5- and 10-year survival showed a significant difference in survival between patients with 15 and 16 points ($p<0.001$). With an increasing MGS value the prognosis deteriorated significantly ($p<0.001$). The patients with a low score had an extremely good prognosis.

Table 5

The distribution of patients and survival at the 5- and 10-year follow-up with respect to MGS points

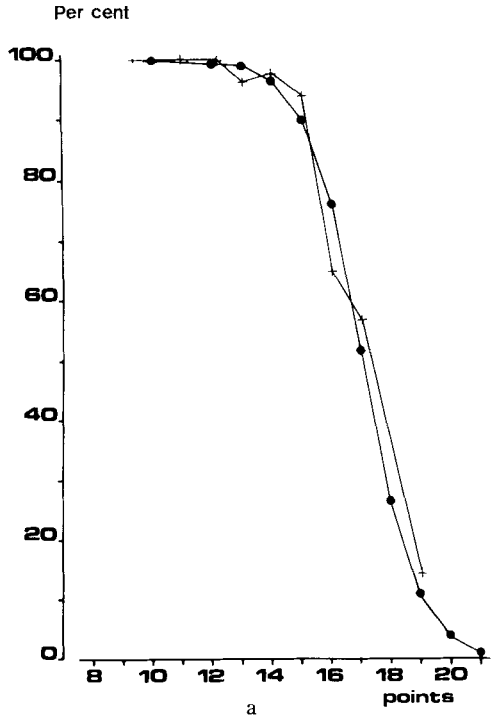
MGS	Total number of cases		Survival	
	5 years	10 years	5 years	10 years
–10	6	6	6	6
11	9	9	9	9
12	23	22	23	22
13	27	27	26	26
14	33	30	32	26
15*	33	33	31	29
16*	17	17	11	10
17	9	8	5	3
18	3	3	1	1
19–	4	4	0	0
	163	159	143	132

* A highly significant difference existed in the 5- and 10-year survival between the patients with 15 and 16 points, χ^2 equals 5.5 and 7.1, respectively.

The relation between the MGS score values and survival is illustrated in Fig. 2. The observed survival rates at 5 and 10 years are given in the figure as well as smoothed logistic regression curves. The goodness of fit between the observed and the predicted curves is striking.

The different items and their grade distribution, and the 10-year survival rates, are shown in Table 6. Significant correlations existed between the grade and the 10-year survival for most of the items; the correlation between the vascular invasion (P7) and the host-cellular response (P8), and survival, was particularly strongly significant ($p<0.001$). However, no significant correlation existed between survival and the differentiation into cell type (P2) or mitosis (P4). Almost always, an increasing MGS score gave a poorer 10-year prognosis.

Multivariate analyses of the prognosis. All results showed that the MGS was strongly correlated to the survival. When each individual factor was analysed



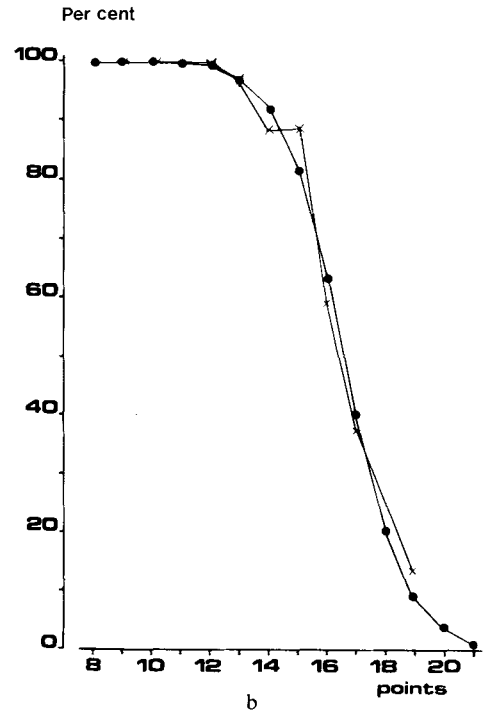


Fig. 2. Observed (x) and predicted (●) survival rates obtained by ogistic regression analysis at a) the 5-year control (163 patients) ınd b) the 10-year control (159 patients) in relation to MGS.

Table 6

Ten-year survival rate for different grades of parameters (n=159)

Parameters	Grade 1	Grade 2	Grade 3
P1 Structure	86% (144)	53% (15)	
P2 Differentiation into cell type	87% (113)	77% (43)	33% (3)
P3 Nuclear polymorphism	84% (55)	92% (59)	71% (45)
P4 Mitosis	83% (24)	85% (84)	80% (51)
P5 Mode of invasion	86% (49)	85% (100)	50% (10)
P6 Stage of invasion	100% (16)	98% (42)	74% (101)
P7 Vascular invasion	91% (92)	86% (42)	48% (25)
P8 Host-cellular response	93% (83)	79% (53)	57% (23)

separately, several with a significant correlation to the 10-year survival emerged: vascular invasion (P7) and tumour-host cellular response (P8). The histologic classification according to ACKERMAN & DEL REGATO (1), and FIGO staging (3), were also significant prognostic factors.

A multiple linear stepwise regression analysis, an AID analysis, and a Cox regression analysis were performed in order to test whether the correlation remained when different variables were analysed simultaneously.

In a *multiple linear stepwise regression analysis* all factors ansalysed were included (Table 7). If the MGS was included it became the dominating variable. A one point increase in MGS corresponded approximately to a 9 per cent decrease in survival. A logistic regression analysis (Fig. 2) indicated that the sigmoid curve ought to be preferred to the linear regression.

If the MGS was excluded from the analysis (Table 7), vascular invasion (P7) was the strongest variable together with host-cellular response (P8), followed by structure (P1) and stage II B (coded 1, the I A–II A coded 0) which showed the highest regression coefficients. The FIGO staging, treatment, histologic classification into cell type or according to ACKERMAN & DEL REGATO or other single MGS items (P1, P2 etc.) did not have the prognostic capacity of the MGS.

The regression analysis was supplemented by an *AID analysis*. There again all factors were included. Fig. 3 demonstrates only the factors which reached

Table 7

Stepwise regression analysis of the 10-year survival/lethality (S/L) rate. Material: 159 patients. Excluded patients: Dead within 5 years after diagnosis, from intercurrent disease, and irradiation treatment less than 60 per cent of the intended dose, incomplete MGS registration or poor biopsy quality. Dependent variable: Survival/lethality rate 10 years after diagnosis (survival = 1, lethality = 0). Program: BMDP2R (2)

Predictor	Regression coefficient	Standard error	t	Beta coefficient
10-year S/L rate including MGS				
MGS	−0.09	0.01	−7.6***	−0.51
Intercept=2.09, R^2=0.28, RSD=0.32				
10-year S/L rate excluding MGS				
Stage II B	−0.20	0.07	−2.87**	−0.20
Structure (P1)	−0.22	0.09	−2.37*	−0.17
Vascular invasion (P7)	−0.16	0.04	−4.60***	−0.32
Host-cellular response (P8)	−0.12	0.04	−3.23**	−0.23
Intercept=1.55, R^2=0.27, RSD=0.33				

Significance: *p<0.05, **p<0.01, ***p<0.001.

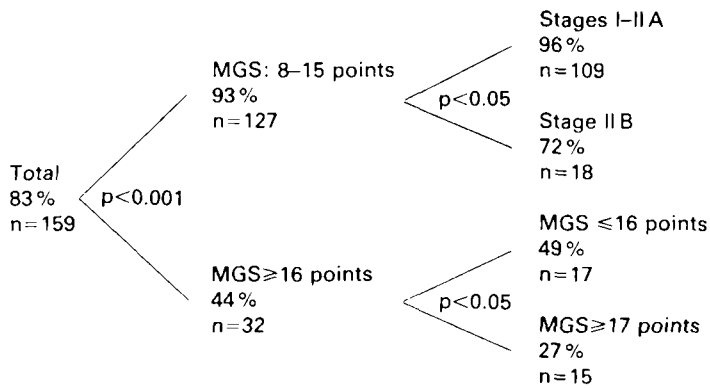


Fig. 3. AID analysis of 10-year survival rates, n=159. Group survival in per cent. All predictors are included. n=number of patients; those dead from intercurrent disease are excluded. Significance analysis (χ^2-test and Fischer's) comparing the groups obtained by the split. First and second splits are mass-significant according to GAVATIN & EKLUND (5).

the specified significant inclusion level. The first two splits considered the MGS level; MGS 8 to 15 p showed 93 per cent 10-year survival in the largest group consisting of 127 out of 159 patients. In the remaining patients, with 16 MGS points or more, 44 per cent survived. There were 15 patients with 17 points or more, and the 10-year survival was only 27 per cent.

The MGS group of 8 to 15 points was split according to stage. Thus stages I A, I B and II A gave 96 per cent survival, stage II B only 72 per cent survival. In the latter group there were, however, only 18 patients. Other factors were not included in the AID tree because they did not reach the mass-significant criterion or were too small. AID analysis as well as regression analysis proved the dominating prognostic capacity of the MGS for 10-year survival. From the AID tree, a low risk patient group with 96 per cent 10-year survival could be identified, namely patients with 15 or fewer points or in stages I A to II A.

The relationship between MGS and survival at,

Table 8

Cox regression analysis with respect to survival. Material: 168 patients. Program: BMDPL2. Predictors: A. MGS alone. B. MGS and Z. C. MGS, P7, P8 and Z. Z is a time dependent variable, T (months) interacting with MGS. The constant 14 corresponds to mean MGS and the constant 4.1 to ln 60. The coefficients in Cox regression analysis correspond to proportional hazard rates

Predictor	Coefficient	SE	t
A. MGS	0.538	0.077	7.0***
B. MGS	0.702	0.139	5.0
Z	0.150	0.107	1.40
C.MGS	0.548	0.167	3.28**
P7	0.309	0.315	0.98
P8	0.448	0.294	1.52
Z=(MGS-14) (lnT-4.1)	0.135	0.108	1.25

Significance: **p<0.01, ***p<0.001.

Table 9

FIGO stage. The ratio between the number of patients dead from the malignant disease at the 10-year follow-up and the initial number (n=159) of patients in combination between MGS and FIGO stages. The table is the basis for the comparison between the correlations to S/L for MGS and FIGO stages (see first line in Table 10)

MGS	I A	I B	II A	II B	Total
≤12	0/19	0/13	0/5	0/0	0/37
13–15	0/4	2/35	2/33	5/18	9/90
16≥	0/0	5/10	10/15	3/7	18/32
Total	0/23	7/58	12/53	8/25	27/159

for instance, 3, 5 and 7 years was also analysed. It could be expected that since the MGS was determined at the time of admission the importance of the MGS measured as the proportional hazard rate would decrease successively with time. To investigate this question, the *Cox proportional hazard regression model* was used (Table 8). Three analyses were performed. The first one (A) included MGS alone. The second (B) included the combination of MGS and time (Z). The Z variable was defined in order to show the change in the prognostic significance of the MGS with time. A positive Z meant that the proportional hazard rate increased with the time after diagnosis. A negative value meant that the importance of the MGS decreased with the time from diagnosis. The regression analysis, considering the excluded cases also, included 168 patients. An additional analysis (C) including the variables mentioned and P7 (vascular invasion) and P8 (tumour-host cellular response) was carried out. The analysis showed that the MGS was the dominating variable (Table 8). No other single variable was significant. The coefficient corresponding to Z was positive, indicating that the importance of the MGS increased with time. This finding, even though not statistically significant, was surprising, probably corroborating the fact that the lethality in carcinoma was higher during the first 5 years than during the latter years of the 10-year period. The coefficients given in Table 8 correspond to proportional hazard rates and illustrate the relative importance of the MGS. A coefficient of 0.54 was obtained for the MGS, disregarding the other variables, and was strongly significant. The coefficient 0.54 implied that an increase in the MGS of one point raised the lethality risk to a hazard rate of 71 per cent. A two point increase in the MGS corresponded to an approximately threefold risk of death from cancer ($1.71^2 \approx 3$). The estimates were, however, very uncertain. The Cox regression analyses performed were in agreement with the analyses carried out on the 10-year material and confirmed the previous impression that MGS was the dominating prognostic factor.

Superiority of the MGS. The ratio between the number of patients who died from malignant disease and the initial number of patients in combination between the MGS and FIGO stages is given in Table 9. The table is the basis for the comparison between the correlations to S/L for MGS and FIGO stages (see the first line in Table 10). In Table 10, the differences between correlations are given. The table shows that the correlation between MGS and S/L (S=0, L=1) was significantly stronger than other correlations to S/L. The significance analyses were performed as in the STENDAHL et coll. report (14) and showed that one half of the differences were highly significant (p<0.001). Some, however, did not reach the 5 per cent significance level. Thus, for the histologic classification according to ACKERMAN & DEL REGATO (1), the vascular invasion (P7), and the host-cellular response (P8), the correlations to S/L were lower than the correlation between MGS and S/L. These correlation differences might, however, have been due to chance. However, after a small modification of the MGS classification (see figures within parentheses in Table 10), significant (p<0.05) differences were obtained also for these predictors. Thus, the superior predictive value of

Table 10

Correlation between MGS and S/L at 10 years compared with the correlation between various variables (X) and S/L and the t-value for the difference (n=159, at most). MGS classified as ≤12 points, 13–15 p, 16 ≥p, given value 1, 2 and 3 points, respectively. The figures within brackets correspond to further subdivision of the 16≥p group; 16 p given value 3 and 17 p≥given value 4

Variable (X)	Code	Difference r−r MGS, S/L X, S/L	t
Stage	I A, I B, II A, II B	0.22	2.53*
Differentiation into cell type (11)	Large cell non-keratinized		
	Large cell keratinized		
	Small cell carcinoma	0.38	4.40***
Classification (1) (n=128)	High differentiation		
	Moderate differentiation		
	Anaplastic carcinoma	0.20	1.95
		(0.25)	(2.28*)
Age	10-year groups	0.40	4.19***
Year of admission	1969, 1970	0.46[1]	3.92***
	P1	0.22	2.00*
	P2	0.25	3.19**
	P3	0.36	4.01***
	P4	0.44	4.34***
	P5	0.34	3.93***
	P6	0.19	2.78**
	P7	0.11	1.63
		(0.17)	(2.38*)
	P8	0.15	1.72
		(0.21)	(2.31*)

[1] Because r_{x1} S/L<0, $(r_{MGS, S/L}) - (r_{x, S/L})$ was constructed.
* 0.01<p≤0.05, ** 0.001<p≤0.01, *** p≤0.001.

MGS is evident from the table. The superiority of the MGS in relation to the clinical stage, illustrated in Tables 9 and 10, is of special interest.

Discussion

The results of this investigation are compatible with earlier results from a similar material (13, 14). The follow-up of the material was extended to 10 years and confirms that the long term prognosis also was very well correlated to the MGS values.

The patient group with low MGS points had an extremely good prognosis. This group represented 1/4 of the patients in the investigation. If the patients with the low point and the moderate point score were aggregated, 93 per cent of the patients were alive at the 10-year follow-up, 95 per cent confidence interval (87%, 97%). The aggregated groups represented 4/5 of the patients in the investigation.

There remained the high point group of patients (32 out of 159) with a prognosis difficult to predict according to the AID tree. The explanatory values obtained by the regression analyses were not particularly high and the similar results appeared in the AID analysis. It is important to find an explanation of why, in one-fifth of the patients, the prognosis remained difficult to predict. In patients with very high scores it is known that the prognosis is unfavourable. In the present material the high lethality among the few patients with 17 points or more was consistent with these earlier findings.

Before the MGS was included in the analyses each factor was analysed separately with respect to the 10-year prognosis. Some factors were significantly correlated with the prognosis. However, these significant results did not remain after the MGS was included.

The superiority of the MGS was expressed by a comparison of the correlation between the MGS and the 10-year survival and the correlation by the other factors. The correlation between the MGS and the survival was highly significant, much higher than the correlation to each single factor, and without exception the differences were significant. Thus, the MGS showed a stronger correlation to the 10-year survival than the clinical stage according to FIGO, when stages I A to II B were analysed. This investigation confirmed previous results (13–15), that the MGS is superior to the established clinical FIGO staging in the prediction of outcome. With respect to predictive power it is open to question whether the MGS classification could be regarded as a suitable substitute for the FIGO staging I to III. This investigation limited to stages I A to II B (n=168) as well as that of STENDAHL et coll. (13), on stages I B to III (n=338) give support to this suggestion. The use of both the malignancy grading system and clinical staging together may allow a somewhat better prediction of the clinical outcome in individual patients as indicated by the AID analysis; even if MGS is superior, the staging seems to have an additional predictive capacity.

The survival analysis showed that the lethality

during the first 5-year period was considerably higher than during the second half of the 10-year period. It was possible to determine whether the prognostic capability of the MGS remained even in this later period. The analysis showed no sign of a time dependent decrease in the prognosticating capacity of the MGS, measured as a proportinal hazard effect.

Only a few pathologists have been involved in the MGS grading. In spite of the registration problems that have been noticed (17), the high survival rates in groups with low and moderate MGS scores are very promising. The present investigation as well as earlier ones are based upon a retrospective material only. By an improvement in the method of fixation and biopsy techniques, estimating of the MGS items becomes more reliable (18).

The original 198 cases had to be reduced to 168 cases due to poor biopsy quality: Thirty patients were excluded because of incomplete registration of one or several items. Parameters for the tumour cell population were almost always possible to evaluate. Items for the tumour–host relationship, especially stage of invasion (P6) and vascular invasion (P7), were often missing. As the most important parameters were lacking, it was considered inadequate to base the MGS on remaining items.

In 31 cases, included among the 168 patients, the representativity of the biopsy was regarded as doubtful. The correlation between the MGS and the outcome was, however, of the same magnitude among the doubtful cases as among the others.

Ten incompletely treated cases were excluded. The limit was set at 60 per cent of the estimated radiation dose in order to eliminate patients with an expected unfavourable prognosis. In the remaining cases, a non-significant correlation between radiation dose and MGS as predictor was observed. The exclusion limit therefore seems to have been suitable.

The comparison of the MGS and the histopathologic staging according to ACKERMAN & DEL REGATO (1) was limited by the fact that the classification was done by many different pathologists and a considerable number of cases were not classified in the primary histopathologic report. Only cases with both MGS grading and an ACKERMAN & DEL REGATO classification could be compared.

The conclusion reached was that the MGS system has a superior prognostic capacity in non-generalized invasive squamous cell carcinoma of the uterine cervix.

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