

U. Rueffer · M. Sieber · M. Stemberg · A. Gossmann ·  
A. Josting · T. Koch · F. Grotenhermen · V. Diehl for  
the German Hodgkin's Lymphoma Study Group  
(GHSG)

## Spleen involvement in Hodgkin's lymphoma: assessment and risk profile

Received: 29 October 2002 / Accepted: 30 January 2003 / Published online: 23 May 2003  
© Springer-Verlag 2003

**Abstract** Diagnostic laparotomy is no longer routinely performed in Hodgkin's lymphoma and noninvasive diagnosis of spleen involvement remains uncertain. In order to assess the probability of splenic involvement based on clinical parameters, we retrospectively analyzed data on patients of the German Hodgkin's Lymphoma Study Group (GHSG) who underwent staging laparotomy and for whom splenic weight and size were available. Our study included 376 patients with Hodgkin's lymphoma who underwent staging laparotomy and splenectomy according to the treatment policy of the GHSG between February 1981 and January 1993. Univariate and multivariate analyses of pretherapeutic clinical characteristics and splenic weight were performed in order to predict the probability of splenic involvement. Computed tomographic (CT) images of 25 patients were available and used to correlate radiological splenic size and pathological splenic weight. In 171 of 376 patients spleen involvement was found. Average weight of the spleens was 258 g ( $\pm 257$ ) ranging from 55 to 3290 g. All spleens with a weight above 2000 g showed disease involvement, while those under 150 g were never involved. In the multivariate analysis, splenic weight ( $p < 0.001$ ), erythrocyte sedimentation rate ( $p < 0.001$ ), and clinical stage ( $p < 0.01$ ) were found to be independently prognostic for spleen involvement. Splenic weight was highly correlated with a spleen index defined as the product of length, width, and thickness measured by CT (correlation coefficient: 0.93). By applying the identified risk factors in

clinically staged patients spleen involvement can be determined. Spleen weight can be estimated with the help of a spleen index. Above an index of 1000 the probability of spleen involvement is higher than 90%. This might be of outstanding importance for patients being scheduled for involved field radiation.

**Keywords** Spleen involvement · Hodgkin's lymphoma · Prognostic factors · Staging laparotomy

### Introduction

Diagnostic laparotomy with splenectomy in Hodgkin's lymphoma has been largely abandoned in recent years due to concerns over impact on survival, delay of the onset of treatment, and long-term consequences of splenectomy [1, 2]. Furthermore, cytostatics are expected to eliminate most of the occult subdiaphragmatic lymphoma. Thus, the increased use of combined modality treatment in early stages of Hodgkin's lymphoma employing chemotherapy and radiotherapy in the involved fields further decreased the need for accurate determination of the pathological stage and to expose the patients to the risks of diagnostic laparotomy.

However, it is still of great interest to determine the intra-abdominal extent of the disease for evaluation and comparison of treatment effectiveness in early clinical stages with the eventual adjustment of treatment modality as a function of subdiaphragmatic conditions.

Options for assessing spleen and liver involvement without staging laparotomy are currently unsatisfactory. The spleen in particular plays a major role in subdiaphragmatic involvement since it is the most frequently involved location in the abdomen and often the only organ affected with Hodgkin's lymphoma [2, 3, 4]. Available imaging techniques do not allow evaluating the presence or absence of disease with the desired accuracy due to high rates of false negative and false positive findings [5, 6, 7, 8].

U. Rueffer (✉) · M. Sieber · M. Stemberg · A. Josting · T. Koch ·  
F. Grotenhermen  
First Department of Internal Medicine,  
University Hospital Cologne,  
Joseph-Stelzmann-Str. 9, 50924 Cologne, Germany  
e-mail: Rueffer@takepart-media.de  
Tel.: +49-221-8207760  
Fax: +49-221-8207761

A. Gossmann  
Department of Radiology,  
University Hospital Cologne,  
Cologne, Germany

Several clinical factors have been found to be prognostic for subdiaphragmatic disease in early clinical stages, i.e., sex, histological subtype, supradiaphragmatic disease patterns, B symptoms, erythrocyte sedimentation rate (ESR), and Karnofsky Index [2, 4, 9, 10, 11, 12]. Some factors, including ESR and mediastinal mass, are already considered when choosing a treatment strategy since they were prognostic for relapse [13]. Splenic weight has also been shown to be predictive for splenic involvement in a study at Stanford University [14], but the probability of involvement never dropped below 20% with small spleens and never exceeded 80% for enlarged organs.

The feasibility of enhancing the prognostic accuracy for splenic involvement using a combination of splenic weight and a range of clinical factors was investigated. Additionally, the possibility of predicting splenic weight from splenic size, as determined with computed tomography, was evaluated.

## Patients and methods

### Selection

A total of 376 patients with Hodgkin's lymphoma for whom pathological spleen weight and relevant clinical data were available were included in this retrospective analysis. All had undergone staging laparotomy and splenectomy before treatment between February 1981 and January 1993, according to the treatment protocols of the HD1 to HD6 studies of the German Hodgkin's Lymphoma Study Group (GHSG). The study group consisted of 249 men (66.2%) and 127 women (33.8%) with ages ranging from 15 to 75 years and an average age of 35.3 years ( $\pm 14.2$ ).

### Statistics

Univariate logistic regression analysis was performed to determine the likelihood of splenic involvement in Hodgkin's lymphoma as a function of the following clinical parameters: erythrocyte sedimentation rate (ESR,  $<50$  mmHg vs  $\geq 50$  mmHg), hemoglobin concentration (Hb,  $<12$  g/dl vs  $\geq 12$  g/dl), sex, clinical stage (early vs advanced), presence or absence of B symptoms, Karnofsky performance score ( $\geq 10$  vs  $<10$ ), mediastinal mass, extranodal disease, and histological subtype ("favorable" vs "unfavorable"). The effect of treatment outcome [complete remission (CR) vs no CR] was analyzed in the same fashion. Nodular sclerosis and lymphocyte predominant histological subtype were regarded as favorable, mixed cellularity and lymphocyte depleted histology were regarded as unfavorable histology. Mediastinal mass was defined as tumor of  $\geq 1/3$  of the maximum thoracic diameter, determined by sagittal radiography. The probability of splenic involvement was also assessed as a function of pathological splenic weight.

Multivariate analysis of prognostic factors was performed with stepwise logistic regression analysis to determine independent prognostic factors. Regression coefficients were used to calculate the probability of spleen involvement depending on combinations of splenic weight and each of the independent prognostic factors.

Partial associations between prognostic factors found in the univariate analysis were ascertained in a hierarchical log-linear model.

### Computed tomography scans

In a subgroup of 25 patients we compared splenic size measured by computed tomography (CT) and pathological splenic weight by Pearson's correlation analysis and linear regression analysis. Preoperative CT had been carried out in 340 patients, and CT images of 25 patients who had been treated at the University Hospital Cologne were available for analysis.

In 16 cases CT examinations had been performed on a Siemens Somatom DR, in two cases on a Siemens Somatom HiQ VD1, and in one case each on a Siemens Somatom Plus S, an Elscint 1800 Excel CT, a Philips Tomoscan 350, a Picker INTL 1200, and a Philips Gyroscan S15. For two patients the model of computed tomograph used was unknown. Section thickness varied between 4 and 18 mm with an average of 9.6 mm. In 23 cases intravenous contrast, oral contrast, or a combination of both was used. The average time gap between CT and laparotomy with splenectomy was 42.1 days.

Splenic size was determined by calculating the splenic index as proposed by Lackner and colleagues [15]. This index is obtained by multiplying the length, width, and thickness of the spleen. Splenic length, width, and thickness were measured according to previously described techniques [15, 16, 17, 18, 19]. Overall spleen length was determined by adding the fractional organ thickness from all sections in which the spleen was visible. The width was determined as the largest diameter in any transverse direction. Spleen thickness is the distance between the inner and outer surface perpendicular to the width, measured at the level of the splenic hilum. When significant differences existed between anterior and posterior parts of the spleen, the mean value was taken according to the method described by Strijk et al. [18].

Statistical significance in regression analyses was accepted at a *p* value of less than 0.05. Calculations were performed using the software SPSS for Windows, version 10.0.

## Results

### Patients' characteristics

There were 249 male and 127 female patients. 192 patients (51.0%) showed an Ann Arbor clinical stage I-II, and 184 (49.0%) were at an advanced clinical stage (CS III-IV). About two-thirds of the patients (61.2%) presented with a favorable histology, mostly nodular sclerosis (52.9%), and one-third (34.6%) showed an unfavorable histology, mostly mixed cellularity (32.4%). Sixteen patients (4.3%) could not be classified according to this classification system. In 70 patients (21.0%) the ESR was  $\geq 50$  mmHg, and in 57 (15.2%) the hemoglobin concentration was below 12 g/l. Additional data on clinical factors are presented in Table 1.

### Spleen involvement/univariate analysis

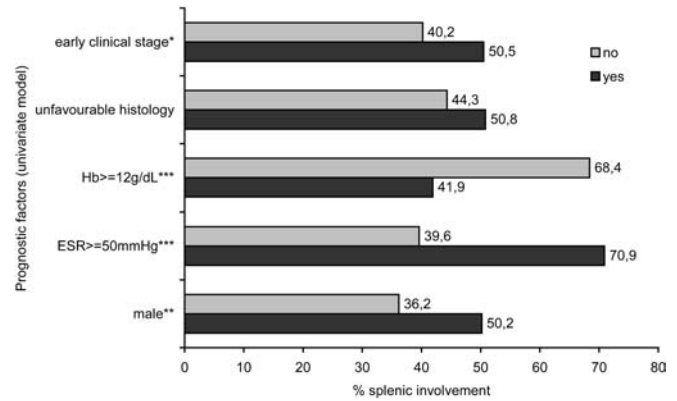
Involvement of the spleen with Hodgkin's lymphoma was observed in 171 of 376 patients (45.5%). Average weight of the spleens was 258 g ( $\pm 257$ ) ranging from 55 to 3290 g, with a median of 195 g. In the univariate analysis, sex ( $p=0.01$ ), clinical stage ( $p=0.05$ ), erythrocyte sedimentation rate ( $p<0.001$ ), hemoglobin concentration ( $p<0.001$ ), and splenic weight ( $p<0.001$ ) had a significant influence on splenic involvement. Splenic involvement was observed more often in men than in women and more

**Table 1** Splenic involvement as determined by laparotomy as a function of selected clinical parameters ( $n=376$ )

	Splenic involvement				<i>p</i> value
	No		Yes		
	No.	%	No.	%	
Sex					
Male	124	49.8	125	50.2	=0.01
Female	81	63.8	46	36.2	
ESR					
<50 mmHg	172	60.4	113	39.6	<0.001
≥50 mmHg	23	29.1	56	70.9	
Hemoglobin					
≥12 g/l	180	58.1	130	41.9	<0.001
<12 g/l	18	31.6	39	68.4	
Histology					
Favorable (NS/LP)	128	55.7	102	44.3	NS
Unfavorable (MC/LD)	64	49.2	66	50.8	
Clinical stage					
Early (CS I+II)	95	49.5	97	50.5	=0.05
Advanced (CS III+IV)	110	59.8	74	40.2	
B symptoms					
No	114	53.3	100	46.7	NS
Yes	91	56.2	71	43.8	
Karnofsky performance score					
<10	93	54.7	77	45.3	NS
=10	102	54.3	86	45.7	
Mediastinal mass					
No	160	55.2	130	44.8	NS
Yes	44	53.7	38	46.3	
Extranodal involvement					
No	154	54.6	128	45.4	NS
Yes	50	54.9	41	45.1	
Treatment outcome					
CR	152	52.4	138	47.6	NS
No CR	53	61.6	33	38.4	

**Table 2** Risks factors for Hodgkin's lymphoma in regression analyses. RR relative risk= $\exp(\beta)$ 

	-2 Log likelihood	Regression coefficient $\beta$	RR	<i>p</i> value
Univariate models				
Sex				
Male		-0.57±0.22	1	<i>p</i> =0.01
Female			0.36	
ESR				
<50 mmHg		1.31±0.28	1	<i>p</i> <0.001
≥50 mmHg			0.71	
Hemoglobin				
≥12 g/l		1.10±0.32	1	<i>p</i> <0.001
<12 g/l			0.68	
Clinical stage				
CSI/II		-0.42±0.21	1	<i>p</i> =0.05
CSIII/IV			0.40	
Splenic weight		0.006±0.001		<i>p</i> <0.001
Multivariate model				
Step 0		498.99		
Step 1	Splenic weight	449.81	0.006±0.001	<i>p</i> <0.001
Step 2	ESR	431.24	1.22±0.29	<i>p</i> <0.001
Step 3	Clinical stage	424.73	-0.60±0.24	<i>p</i> =0.01

**Fig. 1** Prognostic factors for splenic involvement in univariate model. Asterisks mark the level of significance. \* $p \leq 0.05$ , \*\* $p \leq 0.01$ , \*\*\* $p \leq 0.001$ . With unfavorable histology the risk for splenic involvement was slightly increased without reaching statistical significance

often in early clinical stages than in advanced stages (see Table 1). Elevated ESR and decreased Hb were highly significantly associated with the probability of splenic involvement, which increased also with growing pathological splenic weight. Histological subtype, presence of B symptoms, Karnofsky performance score, mediastinal mass, extranodal involvement, and treatment outcome had no significant effect in the univariate analysis.

#### Multivariate analysis

In the multivariate model, which included ESR, hemoglobin concentration, sex, clinical stage, and pathological splenic weight, only three variables were determined to be independent prognostic factors for splenic involvement, i.e., splenic weight ( $p < 0.001$ ), elevated ESR ( $p < 0.001$ ),

**Table 3** Correlations between splenic size gained from CT images and pathological splenic weight

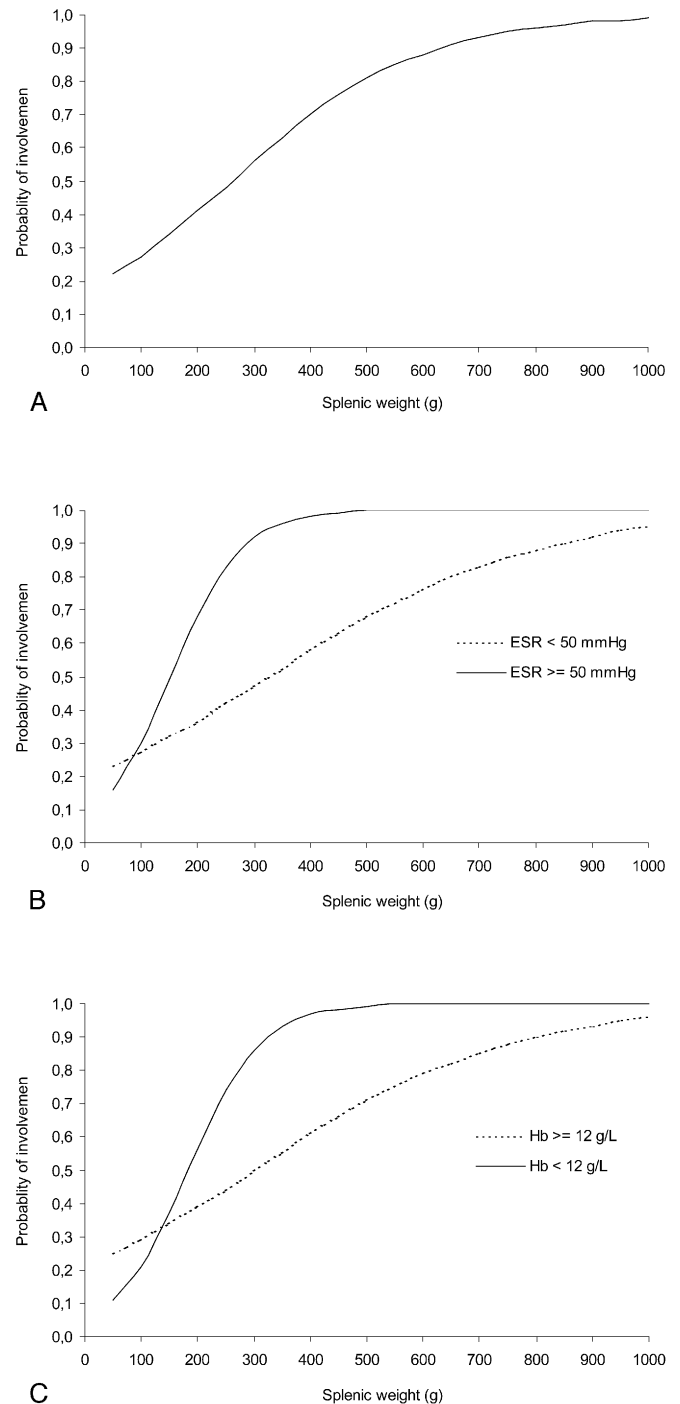
CT parameter	Pearson's correlation coefficient
Splenic length	0.73
Splenic width	0.79
Splenic thickness	0.55
Splenic index (L×W×T)	0.93

and clinical stage ( $p=0.01$ ) (Fig. 1). The most pronounced effects were caused by splenic weight and ESR, while the clinical stage produced only minor improvement of the model (Table 2).

The probability of splenic involvement varied as a function of weight between 22% for a spleen of 50 g and 99% for a spleen of 1000 g, as calculated by the regression coefficients in logistic regression analysis. At an average weight of 300 g, the likelihood of Hodgkin's lymphoma in the spleens of the entire investigated group was 56% (Fig. 2A). Those patients who had a low hemoglobin concentration or an elevated erythrocyte sedimentation rate had a considerably higher risk of about 90% for splenic involvement at a weight of 300 g (86% for Hb <12 g/dl, 92% for ESR  $\geq$ 50 mmHg, Fig. 2B, C) In contrast, only 50% of patients with a normal hemoglobin level and an ESR below 50 mmHg showed involvement at this weight. The effects of clinical stage were less pronounced. In the multivariate analysis the prognostic effect of a low hemoglobin level disappeared. This may be attributable to the partial association of elevated ESR and lowered Hb in a hierarchical log-linear model.

In this model, which included the variables sex, ESR, hemoglobin concentration, clinical stage, and histological subtype significant partial associations between ESR and hemoglobin ( $p<0.001$ ), ESR and sex ( $p=0.007$ ), ESR and clinical stage ( $p=0.05$ ), and between sex and hemoglobin ( $p<0.001$ ) were found. Male patients had an elevated ESR more often than females (23.1% vs 18.9%). Female patients presented more often with lowered hemoglobin (24.6% vs 11%). Patients with elevated ESR more often showed a low hemoglobin concentration than those with normal ESR (43% vs 8.2%) and were more often in advanced clinical stages (58.2% vs 46.7%).

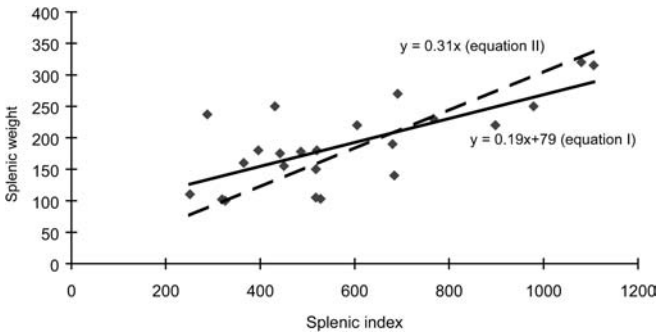
In 8 of the 25 patients (32%) for whom computed tomographic images were available, splenic involvement was detected after splenectomy. In three of these patients focal changes compatible with Hodgkin's lymphoma were identified on CT images, two of whom were confirmed by histological examination, while the third turned out to be a false positive. Average weight was 248 g ( $\pm 281$ ), with a range of 100 to 1560 g. Involved spleens had a considerably higher mean weight of 377 g (range: 155–1560) compared to a mean weight of 176 g for noninvolved organs (range: 100–320). Single splenic dimensions of length, width, and thickness were poorly correlated with the pathological weight, but there was a high correlation ( $r=0.93$ ) with the splenic index as a



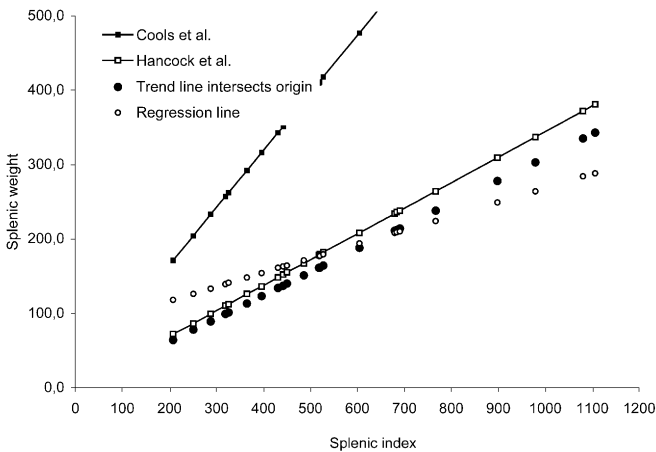
**Fig. 2A-C** Probability of splenic involvement as (A) a function of splenic weight based on univariate logistic regression analysis, (B) depending on splenic weight and erythrocyte sedimentation rate, (C) depending on splenic weight and hemoglobin concentration

product of length, width, and thickness (Table 3). The average splenic index in the 25 patients was 662, with averages for involved and noninvolved patients of 843 and 578, respectively.

Linear regression analysis yielded an equation that allowed derivation of splenic weight from the splenic



**Fig. 3** Splenic weight depending on splenic index. In the two equations  $y$  denotes the splenic weight and  $x$  the splenic index. One of the trend lines represents the regression line (solid line,  $y=0.19x+79$ ), the other trend line intersects the origin (dashed line,  $y=0.31x$ ). Two cases were omitted from the graph, one with a splenic weight of 1560 g and one extreme outlier with a splenic index of 208 and a weight of 300 g



**Fig. 4** Derivation of splenic weight from splenic index ( $L \times W \times T$ ) by different authors compared to the two trend lines established by this study

dimensions (Fig. 3), splenic weight =  $0.19x$  ( $L \times W \times T$ ) + 79 g (Eq. 1). When assuming that the trend line intersects at the origin, it follows Eq. 2: splenic weight =  $0.31x$  ( $L \times W \times T$ ). Figure 3 demonstrates that, despite a good correlation between splenic weight and index, some cases deviate considerably from the respective two trend lines.

Previous authors had developed other equations for correlating splenic index and splenic weight (or volume). We applied several of these equations to the data of our study group (Fig. 4). From a figure in the article of Strijk et al. [18], which presented the correlation between splenic weight and splenic index in 35 patients, splenic weight was estimated to be  $0.56x$  splenic index. Hancock et al. [14] determined splenic weight as  $0.34x$  splenic index, based on data from 94 patients. This correlation is very similar to our second trend line, which intersects at the origin. Two more groups estimated the splenic volume instead of weight, one as to be  $0.77x$  splenic index + 11 [16] and the other as  $0.58x$  splenic index + 30 [17]. As

can be seen in Fig. 4, there was a considerable agreement between our trend lines and the trend line calculated by Hancock et al. [14].

## Discussion

Pathological splenic weight and elevated erythrocyte sedimentation rate were the most relevant independent prognostic factors for involvement of the spleen with Hodgkin's lymphoma among the patients in this analysis. The probability of splenic involvement exceeded 90% if splenic weight reached 300 g in patients with an ESR above 50 mmHg, while the probability of involvement was only about 50% with an ESR below 50 mmHg. Lowered hemoglobin concentration that was significantly prognostic in the univariate analysis disappeared in the multivariate model. Further analysis revealed that ESR and hemoglobin level were significantly correlated, which explains the disappearance of one of the variables.

Our data are in agreement with the findings by Hancock et al. [14] who ascertained splenic weight as the most relevant prognostic factor for splenic involvement, while the significance of clinical parameters in their study differed from ours. The presence of an "unfavorable" histology was the second important prognostic variable in their multivariate model. However, their model did not include ESR and hemoglobin concentration. In our study group the likelihood of splenic involvement only modestly and nonsignificantly increased with unfavorable histology. Differences may be in part explained by a difference in composition between the two cohorts, with a considerably lower percentage of early clinical stages among our patients (51.0% vs 67.6%) and a considerably higher percentage of B symptoms (43.1% vs 27.0%).

In parallel with the decrease in the use of laparotomy and splenectomy for the routine staging procedure, the interest in options for predicting lymphoma by noninvasive techniques again increased. In Hodgkin's lymphoma the spleen is the abdominal location most often affected by occult disease in early stages. In a group of 391 patients of the German Hodgkin's Lymphoma Study Group in limited early clinical stages, 21% had occult abdominal lymphoma detected in laparotomy and the spleen was involved in 86.6%. In 35.4% the spleen was the only subdiaphragmatic location affected [2]. Other groups reported similar results. In a cohort of 1059 patients of the European Organization for Research and Treatment of Cancer Lymphoma (EORTC), less than 10% of all patients in clinical stages I and II with abdominal Hodgkin's lymphoma presented with other subdiaphragmatic locations if the spleen was not involved, while more than 40% presented with other locations if the spleen was involved [4]. In a group of 255 patients diagnostic laparotomy indicated involvement of the spleen in 71% of patients with abdominal involvement [3]. In 62 patients who were upstaged after laparotomy 91% presented with splenic involvement [12].

Hodgkin's lymphoma in the spleen is usually diffuse, and only a small percentage of patients present with nodular lesions, larger than 1 cm in diameter [20]. Focal lesions of the spleen can be diagnosed with high specificity and sensitivity using imaging techniques, but sensitivity drops below 50–60% with diffuse infiltrations [7, 21]. Ultrasound was reported to be of greater sensitivity than computed tomography [21], but sonograms of lymphomas resemble a variety of other malignant and nonmalignant diseases [22]. Laparoscopy is also of limited value in the identification of lymphoma in the spleen [23].

Several clinical parameters and patterns of supradiaphragmatic disease have been found to be independently prognostic for abdominal disease in several studies. Among them the presence of B symptoms [3, 9, 24], elevated ESR [24], unfavorable histological subtypes [2, 3, 9, 10, 24, 25], lowered Karnofsky performance score [2], male sex [3, 10, 11, 25], advanced age [10, 25], absence of mediastinal involvement [2, 10, 25], and left cervical involvement have been identified [2]. As spleen is often affected in patients with subdiaphragmatic presentation of the disease, it is not surprising that some of these risk factors are also prognostic for splenic involvement as found by Hancock et al. [14] and our group.

It had previously been proposed to establish a "prognostic index" for abdominal involvement based on clinical parameters (age, sex, histological subtype, ESR, mediastinal involvement) and assign patients, depending upon their score, to groups with different staging and treatment strategies [26]. However, it was found that even though some of these parameters were associated with the risk of abdominal disease in all studies, several were found to be prognostic in only some studies. This may be due in part to statistical reasons such as differences between the patient groups under investigation and in part to chance.

Our study demonstrates, in agreement with the one of Hancock et al. [14], that splenic weight qualifies as an outstanding prognostic factor for all groups. The prognostic significance of clinical factors will however considerably vary with patient group. Ultrasound, laparoscopy with biopsy, and other diagnostic techniques may eventually be used to further increase diagnostic accuracy. In a prospective analysis with patients suffering from non-Hodgkin's lymphoma and Hodgkin's disease (HD) who received chemotherapy, Daskalogiannaki et al. [17] found a good correlation between changes in splenic size under therapy, as assessed by CT, and indicators of disease status. Thus, changes in splenic size might be useful as an additional indicator of splenic involvement.

The splenic index obtained from computed tomography has been shown to correlate well with splenic weight. Our data, which show a correlation coefficient of 0.93, are in good agreement with those published by other groups [14, 16], who also found correlations of more than 0.90. Additionally, Henderson et al. [27] reported a low day-to-

day variability of 6–10% and an interobserver variability of 4–8% for splenic size measurements with CT.

Our trend line that intersects the origin had a similar slope compared to that of Hancock et al. [14] with the splenic weight being about one-third of the splenic index (0.31 and 0.34, respectively). However, our regression line shows that there might be a tendency to find a comparatively high splenic index for spleens smaller than average and a comparatively low splenic index for spleens larger than average. Our two trend lines intersected at a weight of about 220 g and a splenic index of about 660. At this point, the risk for splenic involvement began to increase considerably in patients with elevated ESR (or low hemoglobin concentration), being about 80% for a weight of 250 g and about 90% for a weight of 300 g. A risk of 90% would be reached with a splenic index of about 880 according to the equation by Hancock et al. [14], with a splenic index of about 970 according to our Eq. 1 and with a splenic index of about 1160 according to our Eq. 2. Thus, we assume that a splenic index of above 1000 in patients with elevated ESR (or low hemoglobin concentration) is highly prognostic for splenic involvement.

For patients who are intended for combined modality treatment, involving multidrug chemotherapy and involved field radiation, the use of splenic index and other prognostic factors for involvement will help define radiation fields and improve the assessment of the effects of involved field radiation on the spleen. Further investigations will be needed to clarify whether this strategy will help decrease the risk of abdominal relapse.

## References

1. Mauch PM (1994) Controversies in the management of early stage Hodgkin's disease. *Blood* 83:318–329
2. Ruffer U, Sieber M, Josting A, Breuer K, Grotenhermen F, Bredenfeld H, Tesch H, Nisters-Backes H, Engert A, Diehl V (1999) Prognostic factors for subdiaphragmatic involvement in clinical stage I-II supradiaphragmatic Hodgkin's disease: a retrospective analysis of the GHSG. *Ann Oncol* 10:1343–1348
3. Trotter MC, Cloud GA, Davis M, Sanford SP, Urist MM, Soong S-J, Halpern NB, Maddox WA, Balch CM (1985) Predicting the risk of abdominal disease in Hodgkin's lymphoma. *Ann Surg* 204:465–469
4. Tubiana M, Henry-Amar M, Hayat M, Burgers M, Gasim M, Somers R, Sizoo W, Van der Schueren E (1984) Prognostic significance of the number of involved areas in the early stages of Hodgkin's disease. *Cancer* 54:885–894
5. DeLaney TF, Glatstein E (1987) The role of the staging laparotomy in the management of Hodgkin's disease. In: DeVita VT Jr, Hellman S, Rosenberg SA (eds) *Cancer: principles and practice of oncology updates*, vol 1. Lippincott, Philadelphia
6. Stomper PC, Cholewinski SP, Park J, Bakshi SP, Barcos MP (1993) Abdominal staging of thoracic Hodgkin disease: CT-lymphangiography-Ga-67 scanning correlation. *Radiology* 187:381–386
7. Plat M, Erk JU (1990) Abdominale Ultraschall Diagnostik bei malignen Lymphomen. *Gastroenterol J* 50:117–123
8. Taylor MA, Kaplan HS, Nelsen TS (1985) Staging laparotomy with splenectomy for Hodgkin's disease: the Stanford experience. *World J Surg* 9:449–460

9. Aragon de la Cruz G, Cardenes H, Otero J, Millan I, de la Torre A, Valcarcel F, Paredes MC (1989) Individual risk of abdominal disease in patients with stages I and II supradiaphragmatic Hodgkin's disease. *Cancer* 63:1799–1803
10. Leibenhaut MH, Hoppe RT, Efron B, Halpern J, Nelsen T, Rosenberg SA (1989) Prognostic indicators of laparotomy findings in clinical stage I-II supradiaphragmatic Hodgkin's disease. *J Clin Oncol* 7:81–91
11. Mauch PM, Kalish LA, Kadin M, Coleman CN, Osteen R, Hellman S (1993) Patterns of presentation of Hodgkin disease. Implications for etiology and pathogenesis. *Cancer* 71:2062–2071
12. Pendlebury SC, Koutts J, Boyages J (1994) Hodgkins disease: clinical and radiological prognostic factors in a laparotomy series. *Australas Radiol* 38:123–126
13. Tubiana M, Henry-Amar M, Carde P, Burgers J, Hayat M, Van de Schueren E, Noordijk E, Tanguy A, Meerwaldt J, Thomas J, De Pauw B, Monconduit M, Cosset J, Somers R (1989) Toward comprehensive management tailored to prognostic factors of patients with clinical stages I and II in Hodgkin's disease: the EORTC Lymphoma Group controlled clinical trials: 1964–1987. *Blood* 73:47–56
14. Hancock SL, Scidmore NS, Hopkins KL, Cox RS, Bergin CJ (1994) Computed tomography assessment of splenic size as a predictor of splenic weight and disease involvement in laparotomy staged Hodgkin's disease. *Int J Radiat Oncol Biol Phys* 28:93–99
15. Lackner K, Brecht G, Janson R, Scherholz K, Lutzeler A, Thurn P (1980) Wertigkeit der Computertomographie bei der Stadieneinteilung primärer Lymphknoten neoplasien [The value of computer tomography in the staging of primary lymph node neoplasms]. *Rofo Fortschr Geb Rontgenstr Nuklearmed* 132:21–30
16. Cools L, Osteaux M, Divano L, Jeanmart L (1983) Prediction of splenic volume by a simple CT measurement: a statistical study. *J Comput Assist Tomogr* 7:426–430
17. Daskalogiannaki M, Prassopoulos P, Katrinakis G, Tritou I, Eliopoulos G, Gourtsoyiannis N (2001) Splenic involvement in lymphomas. Evaluation on serial CT examinations. *Acta Radiol* 42:326–332
18. Strijk SP, Wagener DJT, Bogman MJ, de Pauw BE, Wobbes T (1985) The spleen in Hodgkin disease: diagnostic value of CT. *Radiology* 154:753–757
19. Trusen A, Tschammler A, Wittenberg G, Krahe T (1995) Quantitative computertomographische Milzgrößenbestimmung zur Verlaufsbeurteilung bei malignen Lymphomen. *Rofo Fortschr Geb Rontgenstr Neuen Bildgeb Verfahr* 162:23–28
20. Sandrasegaran K, Robinson PJ, Selby P (1994) Staging of lymphoma in adults. *Clin Radiol* 49:149–161
21. Munker R, Stengel A, Stabler A, Hiller E, Brehm G (1995) Diagnostic accuracy of ultrasound and computed tomography in the staging of Hodgkin's disease. Verification by laparotomy in 100 cases. *Cancer* 76:1460–1466
22. Görg C, Weide R, Schwerk WB (1996) Sonographic patterns in extranodal abdominal lymphomas. *Eur Radiol* 6:855–864
23. Kinsella TJ, Glatstein E (1983) Staging laparotomy and splenectomy for Hodgkin's disease: current status. *Cancer Invest* 1:87–91
24. Mendenhall NP, Cantor AB, Williams JL, Ternberg JL, Weiner MA, Kung FH, Marcus RB, Ferree CR, Leventhal BG (1993) With modern imaging techniques, is staging laparotomy necessary in pediatric Hodgkin's disease? A pediatric oncology group study. *J Clin Oncol* 11:2218–2225
25. Henry-Amar M, Aeppli DM, Abderson J, Ashley S, Bonichon F, Cox RS, Dahlberg SJ, DeBoer G, Dixon DO, Gobbi PG, Gregory W, Hasenclever D, Löffler M, Pompe Kirn V, Santarelli MT, Specht L, Swindell R, Vaughan Hudson B (1990) Workshop statistical report. In: Somers R, Henry-Amar M, Meerwaldt JK, Carde P (eds) *Treatment strategy in Hodgkin's disease: Collque INSERM, Paris, France, vol 196*. John Libbey Eurotext, London, England, pp 217 ff
26. Whillis D, Hancock BW (1989) Staging laparotomy in early Hodgkin's disease: a surgical's view (letter, comment). *J R Coll. Surg Edinb* 34:285–286
27. Henderson JM, Heymsfield SB, Horowitz J, Kutner MH (1981) Measurement of liver and spleen volume by computed tomography. *Radiology* 141:525–527