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Volume, Staging and Grading of Gastro-intestinal Carcinoma—a Population-based Study*

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Abstract—*All cases of the Regional Cancer Registry, North Baden who developed a gastro-intestinal cancer during the period* 1975–1980 *were re-examined according to the following parameters: tumor volume, pT stage, pN stage, grading. In the period considered,* 8424 *cases out of* 14,061 *cases with histologically proven gastro-intestinal cancer could be grouped according to the pT stage. Most of the cases were operated at the pT2 or pT3 stage. Remarkable differences in the different tumor localizations were obtained. Stomach carcinoma had the highest percentage of the pT4 stage* (36.2%), *rectum carcinoma the lowest* (7%). *In all primaries a close coherence of tumor volume and pT stage was noted. Carcinoma at the pT1 stage measured* 20 cm^3 *on average, those at the pT4 stage* 170 cm^3. *No coherence of staging and age of the patients could be obtained. Younger patients showed a higher percentage of undifferentiated carcinoma than older patients. Survival data could not be obtained due to the data protection law.*

INTRODUCTION

THE PURPOSE of this report is to give some population-based data on the expansion of tumors at the time of surgical treatment. In addition, some morphological criteria, such as inflammatory infiltrations, curative excision, etc., are noted.

It is well known that the TNM stage of carcinomas is of importance regarding the prognosis and survival of the patients [1, 2]. Although the TNM classification is used by the majority of hospitals and although it has a world-wide distribution, the pTNM stage of carcinomas given by the pathologists is not yet utilized by institutes of pathology at a satisfying level. Unlike other localizations, the pTN stage of colo-rectal carcinomas differs from the TN stage. It is based upon the tumor infiltration into the different layers of the gut. This classification, based upon the Dukes classification [3, 4] and its modifications by Kirklin *et al.* [5], has its value especially for advanced tumor stages (pT2–4). On the other hand, it was impossible for these authors to show an influence of their classification in early colo-rectal cancer (pT1) due to the lack of cases. In former studies dealing with prognostic parameters for the patients' survival the classification of colo-rectal carcinomas was performed mainly in two stages: invasive and non-invasive carcinomas [5, 6].

Turnbull *et al.* [7] included an additional category (distant metastases) in the Dukes classification which was modified by several authors [9–14]. Tumor expansion and lymph node involvement were separated by this classification.

The data in this paper are based upon the data of six patho-anatomical institutes, all located in the district of North Baden. They describe the distribution and expansion of gastro-intestinal carcinomas according to the pTN stage as reported by pathologists. In comparison to earlier data [4, 6, 7], the diagnostic situation of the colorectal carcinomas has changed extremely. Most of the patients suffering from rectal

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carcinomas were able to be treated at the pT1 stage.

MATERIALS AND METHODS

Since 1971 the Regional Cancer Registry of North Baden has registered all patients with histologically proven cancer of the gastro-intestinal tract. The crude and age-standardized incidence rates are comparable to incidence data of similar areas (Saarland, Hamburg, Denmark) [15]. All cases registered during the period 1975–1980 were analyzed in detail. The pT and pN stages, the tumor volume, and grading and inflammatory infiltrations of the tumors were revealed from the histomorphological findings as described by the pathologist. Only resection specimens were taken into account. The organization of the registry, its geographical distribution, etc., is described elsewhere [15–17]. Since it is prohibited by law to compare registered cases with mortality data, no survival data could be obtained. The pTN classification of esophageal, stomach and colo-rectal carcinomas was performed according to the rules of the UICC [18]. The pT classification of carcinomas of the small intestines was performed according to the rules proposed by the UICC for carcinomas of the stomach, colon or rectum, since no pTN classification of the small intestines had been introduced until now. The lymph node involvement of carcinomas of the small intestines was classified according to the pN rules for stomach carcinomas. If a lymph node involvement was found 3 cm or less from the borderline of the primary, the lymph node metastasis was classified as in the pN1 category. If para-aortal or hepato-duodenal lymph nodes were involved, this category was classified as pN3. The tumor volume was computed according to the documented three perpendicular diameters or according to explicit noted tumor volume.

RESULTS

In the period considered a total of 14,061 cases were registered. A detailed pT stage could be evaluated in 8424 cases (59.9%) (resection material only). In the missing cases no resection was performed or a pT stage could not be evaluated from the histomorphological description. The detailed pT stage of the different topographies is shown in Table 1. The percentage of pT stages obtained differs remarkably from the esophagus to the colon. In esophageal carcinomas only 24% of the cases could be classified according to a pT stage; in colon carcinomas this percentage rises up to 78%. The corresponding infiltration of the tumors into the different layers of the gut is shown in Table 2. Carcinomas of the small intestines were the most advanced. Forty percent of the documented carcinomas of small intestines showed a tumor infiltration into the surrounding tissue.

The tumor volume, grouped according to the pT stage, is shown in Table 3. In different organs the tumor size is very similar. Carcinomas at the pT1 stage showed a tumor volume of about

Table 1. pT stage of gastro-intestinal cancer cases vs primary site

	Esophagus		Stomach		Small intestines		Colon		Rectum	
pT-stage	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%
pTis	4	3.4	19	0.8	–	–	19	0.6	40	1.7
pT1	19	16.2	489	20.7	13	11.4	343	10.0	616	25.5
pT2	24	20.4	491	20.8	23	20.2	1101	32.2	838	34.7
pT3	71	60.0	508	21.5	19	16.6	1319	38.6	750	31.1
pT4	–	–	854	36.2	59	51.8	635	18.6	170	7.0

Regional Cancer Registry, North Baden 1975–1980 ($n = 8424$).

Table 2. Tumor infiltration of gastro-intestinal cancer vs primary site

	Esophagus		Stomach		Small intestines		Colon		Rectum	
Tumor invasion	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%
Mucosa	7	6.0	239	10.1	3	2.6	187	5.5	267	11.1
Submucosa	16	13.5	269	11.4	10	8.8	175	5.1	389	16.1
Muscularis	24	20.3	491	20.8	23	20.2	640	18.7	644	26.7
Serosa			508	21.5	19	16.6	461	13.5	194	8.1
Fatty tissue* and continuous structures	71	60.2	854	36.2	59	51.8	1954	57.2	920	38.3

Regional Cancer Registry, North Baden, 1975–1980 ($n = 8347$).
*Outside the serosa.

Table 3. pT stage of gastro-intestinal cancer vs tumor volume

	Esophagus (cm^3)	Stomach (cm^3)	Small intestines (cm^3)	Colon (cm^3)	Rectum (cm^3)
pT1	13 ± 5	17 ± 3	21 ± 3	22 ± 4	18 ± 2
pT2	31 ± 15	61 ± 5	35 ± 12	55 ± 7	45 ± 9
pT3	102 ± 10	96 ± 8	100 ± 13	99 ± 14	79 ± 14
pT4	-	152 ± 17	155 ± 20	166 ± 18	184 ± 16

Regional Cancer Registry, North Baden, 1975–1980 (confidence interval, $\alpha \leqslant 0.05$; $n = 2364$).

Table 4. pT stage of gastro-intestinal cancer vs pN stage

	pT1		pT2		pT3		pT4	
	n	%	*n*	%	*n*	%	*n*	%
			Esophagus ($n = 64$)					
pN0	3	75.0	9	69.2	6	12.8		
pN1	1	25.0	4	30.8	39	83.0		
pN2	-	-	-	-	2	4.2		
			Stomach ($n = 1619$)					
pN0	209	86.0	218	55.5	177	41.3	123	22.2
pN1	31	12.8	134	34.1	156	36.4	198	35.7
pN2	1	0.4	28	7.1	52	12.1	88	15.9
pN3	2	0.8	13	3.3	44	10.2	145	26.2
			Small intestines ($n = 53$)					
pN0	1	50.0	7	58.3	4	66.7	9	27.3
pN1	1	50.0	5	41.7	2	33.3	8	24.2
pN2	-	-	-	-	-	-	1	3.0
pN3	-	-	-	-	-	-	15	45.5
			Colon ($n = 2709$)					
pN0	129	91.5	673	70.7	712	59.1	173	42.1
pN1	12	8.5	250	26.3	461	38.3	153	37.2
pN4	-	-	29	3.0	32	2.6	85	20.7
			Rectum ($n = 1628$)					
pN0	158	90.8	503	74.3	348	51.3	38	38.4
pN1	16	9.2	174	25.7	305	45.0	30	30.3
pN4	-	-	-	-	25	3.7	31	31.3

Regional Cancer Registry, North Baden, 1975–1980.

20 cm^3, those of the pT2 stage about 50 cm^3. Tumors of the pT3 stage measured about 100 cm^3 and tumors of the pT4 stage 160–170 cm^3. In general the tumor volume doubles from one to the next higher pT stage.

The pT stages and the corresponding pN stage are shown in Table 4. About 90% of carcinomas at the pT1 stage showed no lymph node involvement (pN0 stage). This percentage is similar for different localizations. Regarding other pT stages (pT2–4), the situation is different. Although the tumor volume is about the same, the percentage of lymph node involvement differs, especially between colo-rectal and stomach carcinomas. Colo-rectal carcinomas show a combined pN0–pT4 stage in about 40%, stomach carcinomas in only 22%. The difference is significant ($\alpha \leqslant 0.01$). Stomach carcinomas are more likely to involve regional and distant lymph nodes than carcinomas of the colon or rectum. This observation also holds true for other pT stages (pT2, pT3).

An explicit description of possible tumor infiltration of resection borderline or curative resection was documented in about 60% of the resection specimens. The percentage of the possible curative resections depends upon the pT stage and the localization (Table 5). About 95% of carcinomas of the colon and rectum were operated as curative resections. For carcinomas of the stomach this percentage holds true only in the case of the pT1 stage.

The grading of the carcinomas grouped according to the major gastro-intestinal sites (stomach, colon, rectum) and in accordance to the

Table 5. pT stage of gastro-intestinal cancer vs tumor infiltration of resection borderline

	pT1		pT2		pT3		pT4	
	n	%	*n*	%	*n*	%	*n*	%
			Stomach ($n = 1266$)					
Curative	145	92.4	288	84.5	279	79.5	323	77.5
Not curative	12	7.6	53	15.5	72	20.5	94	22.5
			Small intestines ($n = 35$)					
Curative	3	100.0	8	88.9	7	100.0	15	93.8
Not curative	-	-	1	11.1	-	-	1	6.2
			Colon ($n = 1871$)					
Curative	40	99.2	598	98.5	862	97.6	221	92.1
Not curative	1	0.7	9	1.5	21	2.4	19	7.9
			Rectum ($n = 1201$)					
Curative	178	97.3	440	95.9	482	96.2	52	89.7
Not curative	5	2.7	19	4.1	19	3.8	6	10.3

Regional Cancer Registry, North Baden, 1975–1980.

Table 6. Grading of gastro-intestinal cancer vs age of cancer patients

	Esophagus		Stomach		Small intestines		Colon		Rectum	
Inflammation	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%
None	3	3.3	21	2.5	2	8.0	20	2.6	11	1.2
Moderate	45	49.5	363	43.0	15	60.0	291	38.0	379	40.6
Severe	39	42.9	431	51.1	6	24.0	360	47.1	472	50.6
Tumor borderline	4	4.3	29	3.4	2	8.0	94	12.3	71	7.6

Regional Cancer Registry, North Baden, 1975–1980 ($n = 2658$).

age of the patients is shown in Fig. 1. The majority of the carcinomas were described as moderately differentiated, but differences according to the age and primary sites exist in general. Stomach carcinomas are less differentiated than carcinomas of the colon or rectum. Older patients showed a higher percentage of well-differentiated carcinomas than patients at a younger age. This holds true especially for carcinomas of the stomach.

No differences could be found regarding inflammatory infiltrations within the tumor or at the tumor borderline (Table 6). Most of the carcinomas showed a moderate-to-severe infiltration of lymphocytes, plasma cells and macrophages.

DISCUSSION

Although individual factors certainly play an important part in the therapy and prognosis of cancer, there is need for standardized data and standardized therapy schemes. From the clinical point of view the TNM classification is well known and is used for standardized therapy schemes in different malignancies [17, 18]. Although the morphological diagnosis is the basis of all cancer treatment, the pTNM stage for most cancer types is considered only as an appendix to the clinical classifications. In the case of gastro-intestinal cancer this does not hold true, probably due to the early work of Dukes [3], Miles [19] and Lockhart-Mummery [20]. The pTNM classification used in this paper is based upon the classification of the UICC [16]. It is a purely morphological classification. No biological or immunologic parameters are taken into consideration.

Due to the data protection law in West Germany, we are unable to give survival data. Our population-based data describe only the extension of gastro-intestinal cancer at the time of surgical treatment. Death certificates are filed without personal identifications. The offices of public registration are not willing or able to handle the names of dead people, although those data are published regularly in local newspapers.

The pT stages shown in Table 1 are based upon a total number of 14,061 cases. In 69% the morphological descriptions of resection specimens are either filed exclusively or in addition to biopsy data. In 60% of the cases a detailed description of infiltration into the gut was documented (8424 cases).

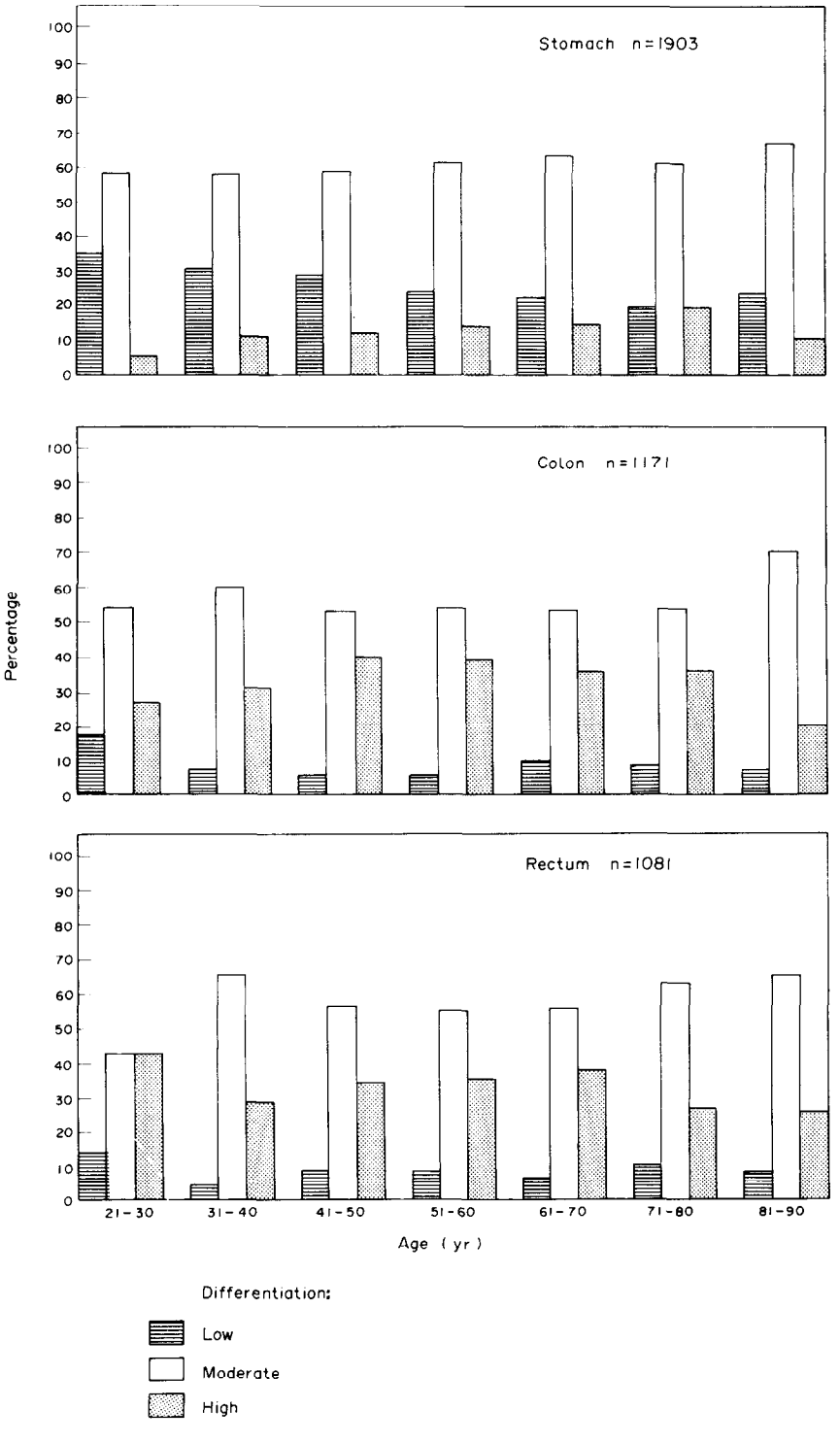

Fig. 1. Regional Cancer Registry, North Baden, 1975–1980: grading vs age of patients.

An explicit description of the pTN stage was given in only 703 cases (5%). Infiltrations of inflammatory cells into tumor tissue or at the tumor borderline were described in 2658 cases (19%). Lymph node involvement by tumor cells was noted or excluded in 4122 cases (29%).

Esophagus

The sex ratio of esophageal carcinoma in the data of our registry (4.7:1, males:females) is in accordance with other authors [21–24]. Only in 118 cases are resection specimens registered. The majority of these cases (71 cases or 59.2%) already showed a tumor infiltration into the surrounding connective tissue and continuous structures (pT3). A carcinoma *in situ* was evident in only four cases (3.4%). These data in comparison with the data reported by Iizuka *et al.* [25], who gave a 5-yr survival rate of 18.6% at the pT2 stage and a 5-yr survival rate of 0% for the pT3 stage, explain

the poor prognosis of patients suffering from esophageal carcinomas. The lymph node involvement of esophageal carcinoma is similar to the carcinoma of the stomach. The average tumor volume of esophageal and stomach carcinomas are also similar at different pT stages.

Stomach

Stomach carcinomas cover about one-third of all gastro-intestinal cancer. Forty percent of them could be operated at the pT1 or pT2 stage, but another 36% only at the pT4 stage (Table 1). The sex ratio in our material is 1.3:1 (males:females), in accordance with the data of others [22, 26, 27]. The rate of 22% of carcinomas *in situ* or pT1 carcinomas is quite low compared to data given by other authors.

Evans *et al.* [28] reported 36% of gastric carcinomas at an early stage. In a cancer screening program for gastro-intestinal carcinomas in Japan [29] this rate was increased, at 43%, at an early stage. The tumor volumes of gastric carcinomas within the pT stages are similar to the tumor volumes of colon or rectum carcinomas. The time of tumor growth up to the pT1 stage has been computed to be 2.5–3 yr. It takes an additional year to develop from the pT1 to the pT2 stage. Another 6 months elapse before it develops from the pT3 to the pT4 stage. The computations were performed using the following presumptions: the tumor growth function described by Kob *et al.* [30] was used as well as growth velocities of lung metastases of gastro-intestinal carcinomas, which show a tumor volume of 1 cm^3 after a period of 200 days on average [30], and an average duplication time of 200 days [31].

The lymph node involvement of gastric carcinomas in advanced pT stages was found in a higher percentage than carcinomas of the colon and rectum. A pN2 and pN3 stage at the pT1 carcinoma stage was found in only 1.2%. pT4 carcinomas showed these pN stages in more than 40%. While Beger *et al.* [24] found the N0 stage in 87.2% of their material, Kennedy [32] found the N0 category in only 23.5%. The major borderline in order to confirm or exclude lymph node metastases is the mucosa muscularis. If a cancer already infiltrates the sub-mucosa, lymph node metastases are found in 18–47% [33–35].

A possible curative resection could be performed in the majority of cases (Table 5). Possible tumor masses were left in 7.6% at the pT1 stage and in 22.5% at the pT4 stage. According to Beger *et al.* [24], the best predictor of survival is the N stage. These authors gave a 10-yr survival rate of 79% at the N0 stage but only 33.3% at the N3 stage.

In our material undifferentiated stomach carcinomas are found to be more frequent in younger patients (50 yr or younger). The opposite holds true for highly differentiated carcinomas. The majority of the carcinomas was described as moderately differentiated. Therefore these data show only a tendency. Using the classification of Laurén [36] or Ming [37], the data are in accordance with the well-known fact that carcinomas of the diffuse type are more frequent at younger ages (average age of patients: 59–62 yr, males; 60–64 yr, females; confidence interval, $\alpha \leqslant 0.05$), while those of the intestinal type are seen to be more likely in older patients (average age of patients: 65–67 yr, males; 67–70 yr, females) [14].

Small intestines

Cancer of the small intestines is as throughout the world rare in North Baden. The classification of 114 carcinomas of the small intestines revealed that most of the carcinomas (52%) were at the pT4 stage. The tumor volume of the pT4 stage is very similar to that of the pT stages of carcinomas of the colon, rectum and stomach. The same holds true for lymph node involvement. In the case of carcinomas of the small intestines a retrospective pN classification could be performed only in about 50% of the cases. At the pT4 stage nearly half of the carcinomas showed pN3 involvement. According to Kayser [14], clinical symptoms indicated that carcinomas of the small intestines grow very rapidly. Other authors reported an infaust prognosis of patients with carcinomas of the small intestines [38].

Colon, rectum

Colon and rectum carcinomas have a high incidence in North Baden [39]. These carcinomas have similar tumor volumes at the same pT stage (Table 3) but quite different distributions of the pT stages at the time of surgical treatment. The pT1 stage of rectum carcinomas (25.5%) is the most frequent of all pT1 stages in gastro-intestinal carcinomas. Only 7% of rectum carcinomas were operated on at the pT4 stage. Regarding the pT stage, colon carcinomas are worse, being similar to carcinomas of the small intestines. Stock *et al.* [40] reported that 301 out of 456 cases had to be classified in the pT4 category; only 21 of his cases were operated on at the pT1 stage. The positive differences in our data can be explained by the high percentage of coloscopic examinations in North Baden. About 50% of our cases were histologically proven by biopsies to be followed by resection. The frequency of biopsies for rectum carcinomas is about 85%. The lymph node involvement at different pT stages is very similar for colon and rectum carcinomas. The

advanced pT4 carcinomas of the rectum showed a higher percentage of the pN4 stage (31.4%) than carcinomas of the colon (20.7%). The difference is not statistically significant. Our data are in agreement with the data published by Bokelmann [41], who found a rate of pN4 stage of 13.6% at the pT1 and pT2 stages. The grading of the carcinomas revealed highly differentiated carcinomas (G1) in about 35% of both rectum and colon carcinomas. Only 8% were described as low, or undifferentiated, tumors. This is in accordance with previous data, which showed an increase of the differentiation of carcinomas within the gut from the esophagus to the colon-rectum [14].

CONCLUSIONS

Our data revealed similarities (tumor volume) and differences (pT and pN stages, grading) of gastro-intestinal cancer according to the primary site. The tumor volume of all carcinomas is very similar if grouped according to the pT stage [16]. The lymph node involvement, depending on the pT stage, is similar in carcinomas of the colon and rectum but different in carcinomas of the stomach, small intestines and esophagus. Highly differentiated carcinomas are more frequent if situated in the colon or rectum than in the stomach or esophagus. The data presented describe the medical diagnostic features in North Baden (1975–1980).

If the primary site of carcinomas is easy to locate by diagnostic procedures (e.g. the rectum) a good chance to treat the patients at a non-advanced stage exists. But even in the case of more difficult primary sites, progress in diagnostics can be seen compared to data reported 30 yr ago.

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