10 Years Endoscopic Diagnosis of Early Gastric Cancer in Europe

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Summary. In two different inquiries concerning the diagnosis of gastric cancer and especially early gastric cancer (E.G.C.) (comprising the years 1968–1977) we collected all over Europe 872,376 gastroscopies with 2832 E.G.C. (0.3%). For 739,360 gastroscopies a total of 39,953 gastric cancers was reported of which 2475 were E.G.C. (6.2%). One E.G.C. was found in 308 gastroscopies. The ulcerating types (IIc and III) were the most frequent ones. The antrum, including angulus and pylorus, and the Magenstraße may be considered as zones of predilection. 94% of all patients with an E.G.C. have had complaints for several months or years before. Gastro-intestinal bleeding is found in 11.4% of the patients over the age of 40. 40% of E.G.C. were found in women, 60% in men. E.G.C. is the most frequent from the 6th to the 8th decade of age. Diagnosis of cancer is made by biopsy and/or cytology. The accuracy of diagnosis correlates with the number of biopsy particles from the lesion. A previous, carefully done X-ray examination increases the efficiency of gastroscopy in finding an E.G.C.

Key words: Early gastric cancer (E.G.C.) — Gastric cancer — Gastroscopy — Symptoms of E.G.C. — Incidence

The first publication concerning gastric mucosal cancer was made by Versé [25] in Leipzig in 1907. In 10,000 successive autopsies he found 12 mucosal gastric cancers. Between 1930 and World War II two scientists were essentially concerned with the early stage of gastric cancer: Konjetzny (Germany) [12, 13, 14] and Gutmann (France) [4, 5, 6]. Obviously, these efforts were interrupted through World War II and only in 1956 Gutmann [7] could publish further experiences.

Versé and Gutmann defined the early stage of gastric cancer as "carcinomatous changes limited to the mucosa".

The papers by Versé were forgotten and those by Gutmann not accepted in the medical world, except in France.

The diagnosis of E.G.C. was promoted with the introduction of the gastroca-mera by the Japanese [22] and the fiberscope by the Americans in 1960 [9]. Now, the gastroenterologist was able for the first time in history to describe the mucosal lesions in their form, color, extension, and consistency, just like a dermatologist the skin. These lesion could be photographed and biopsied.

In 1962, the Japanese Society of Endoscopy called the mucosal stages of gastric carcinoma "early gastric cancer" and it was defined as a cancer limited to the mucosa and the submucosa, with or without regional lymph node metastases [15, 20]. The world "early" includes a factor of time and this is, as we know today, wrong. The expression "mucosal gastric cancer" would be much more appropri-ate [10a].

The diagnosis of E.G.C. is based upon the exact histologic examination through the pathologist who needs a subtile preparing of the resected specimen according to the method of Nakamura [17]. The differentiation between an E.G.C. and a fully developed, all layers penetrating gastric cancer is justified since the prognosis is completely different. The 5-year-survival in case of a fully devel-oped gastric cancer is below 10%, in case of a cancer limited to the mucosa it is 93–99% and 88–93% if the submucosa is infiltrated [8]. If regional lymph node metastases are present, the survival decreases to 79% [11].

Methods

Each member of the national societies of gastrointestinal endoscopy was contacted twice. In 1974, we sent out 2700 questionnair and 261 or 10% were returned duly filled out. In 1978 more than 4000 questionnaires were mailed out and we received 270 answers or 7%.

With our inquiries we requested the total number of gastroscopies in the years 1968–1977, the number of endoscopically diagnosed gastric cancers, the number of E.G.C., their type and location, and information about the procedure in order to diagnose a cancer. In 1974, additional information was requested about the number of biopsies taken in suspected lesions, about cytologic examination and clinical data about each case of E.G.C. as sex, age and symptoms.

In 1978, only 204 of 270 examiners were able to communicate the number of endoscopically diagnosed gastric carcinoma.

Results

For the years 1968–1977 the inquiries yielded a total of 872,376 gastroscopies with 2832 E.G.C. (0.3%) or a total of 739,360 gastroscopies with 39,953 gastric carci-noma, of which there were 2475 E.G.C. (6.2%).

Table 1 shows the number of gastroscopies, of diagnosed E.G.C., the ratio E.G.C./gastroscopies and the adjusted death rate of gastric cancer in different countries [1].

The highest death rate of gastric cancer is found especially in the countries of Eastern Europe, in Germany (BRD) and Italy, the lowest death rate in the coun-tries along the coast. There can be found a relation between the frequency of gastric cancer in a country and its ratio E.G.C./gastroscopies. Norway and Portu-gal are exceptions confirming the rule. From a total number of 2832 E.G.C. the types were indicated in 2185 cases (Table 2). Type I was found 456 times (21%), Type IIa 252 times (12%), Type IIb 252 times (12%), Type IIc 645 times (29%) and Type III 580 times (26%). The Types IIc and III were the most frequent ones.

Table 1. Summaring the figures of 10 years of endoscopic diagnosis of early gastric cancer in Europe and indicates the name of the country according to the international car plates, the total of communicated endoscopies as well as the number of E.G.C. found during this 10-year-period. The ratio E.G.C./Scopies indicates how many gastroscopies were needed in order to find one case of E.G.C. in the respective country. It can be seen that in countries with a high death rate on gastric cancer, an E.G.C. is found more frequently than in those with a low death rate

Country	Endoscopies	E.G.C.	Ratio E.G.C./ Scopies	Age adjusted death (1) rates per 100000		Average age 1968–1973
				Male	Female	
H	52, 250	293	1: 178	40.17	20.63	55
PL	40, 391	126	1: 321	38.34	16.48	55.9
CS	17, 402	33	1: 527	36.28	18.33	–
A	38, 669	149	1: 260	35.82	19.55	64.3
P	11, 167	56	1: 199	34.67	18.73	61
B	828	3	1: 276	31.77	18.93	–
D	259, 673	869	1: 299	30.59	16.63	59.9
SF	27, 448	33	1: 832	30.5	15.45	61
I	84, 461	363	1: 233	30.42	15	53.4
E	34, 384	97	1: 354	27.11	14.81	58.6
NL	17, 048	32	1: 533	23.28	11.72	60.7
YU	26, 855	64	1: 420	22.53	11.65	52.7
N	15, 565	75	1: 208	21.78	9.86	68.9
IRL	7, 732	18	1: 430	21.73	14.4	–
CH	55, 843	155	1: 360	21.19	11.31	57.8
GB	36, 763	45	1: 817	21.12	10.01	54.3
F	76, 579	252	1: 304	17.96	8.15	59.8
S	24, 976	70	1: 357	17.48	9.68	–
DK	24, 913	20	1:1246	16.91	9.49	63.8
GR	843	19	1: 44	14.28	7.97	55
IS	1, 874	6	1: 312	?	?	?
USSR	3, 732	22	1: 170	?	?	?
DDR	12, 980	32	1: 406	?	?	?
Total:	872, 376	2, 832	1: 308			

Elster communicated the results of 225 E.G.C. with approximately the same distribution (Table 2) [2].

The distribution of the different types in the stomach is uniform.

The location shows 1.5% in cardia, 44% in the fundic region and the corpus, 22% in the gastric angle, 31% in antrum and 1,5% in the pylorus. 44% were located in the Magenstraße (Fig. 1).

In the first inquiry, 1968–1973, we received *clinical data* of 658 patients.

Sex and Age (Table 3)

60% of all E.G.C. were found in men and 40% in women. E.G.C. occurs in adolescents to old age patients. E.G.C. is most frequent in males in the 6th and 7th decade, in females in the 7th and 8th decade. The average age varies from one country to another. It is remarkable that there is a difference in the average age

Table 2. Frequency of types in E.G.C.

	1968–1977 $n = 2185$	Elster $n = 225$
Typ I	20.9%	13.4%
II a	11.5%	10.3%
Typ II II b	11.5%	14.3%
II c	29.5%	43.3%
Typ III	26.6%	18.7%

E.C. IN EUROPE 1968-77
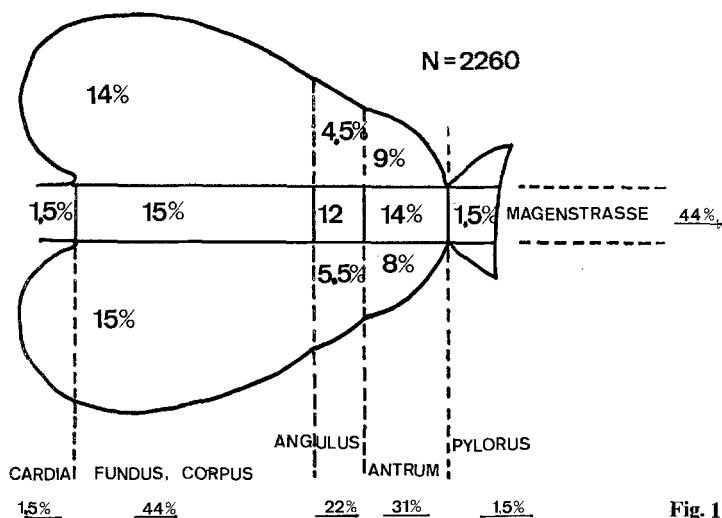
Fig. 1

between North and South Europe. In Norway, e.g., E.G.C. appears on the average 10 years later than in Italy (Table 1).

Symptoms

In 649 of 658 patients we obtained information about the anamnesis (Table 4). Of these patients 94% have had complaints. Uncharacteristic abdominal pains were most frequent with 69.9%; 26,8% of all patients have had postprandial pains, 25.8% nausea and 23.8% fasting epigastric pains. It seems remarkable that 33.6% of all patients have had a loss of weight and 23.4% anorexia. Hematemesis or melena were reported in 73 cases or 11.2% (Table 5). While uncharacteristic complaints had been present up to 24 months before gastroscopy, hematemesis or melena often, but not always, were the reason for urgent endoscopic examination.

Below the age of 40 (52 patients), hematemesis and melena were only present in 3 cases (5.7%). From the 5th to the 9th decade (596 patients), the frequency of gastric hemorrhage was increasing: 70 patients or 11.7% showed hematemesis or

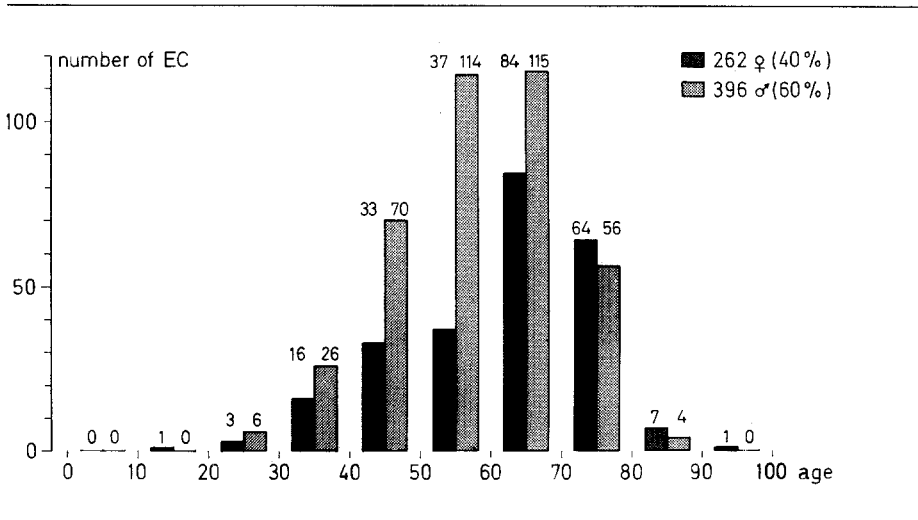**Table 3.** Age and sex. 658 cases of early cancer of the stomach in Europe 1968–1973

Table 4. $n = 649$ Frequency of symptoms in E.G.C.

Abdominal pain	$454 \times (69.9\%)$
Weight loss	$218 \times (33.6\%)$
Postprandial pain	$174 \times (26.8\%)$
Nausea	$168 \times (25.8\%)$
Fasting epigastric pain	$155 \times (23.8\%)$
Anorexia	$152 \times (23.4\%)$
Belching	$57 \times (8.8\%)$
Hearth Burn	$56 \times (8.6\%)$
Melena and Hematemesis	$73 \times (11.2\%)$
No symptoms	$37 \times (5.7\%)$

melena (Table 5). There is no relation between the complaints and the different types of cancer, except the fact that hemorrhage is twice as frequent in lesions with a mucosal defect (Types IIc and III).

Biopsy (Tables 6 and 7)

We received information about biopsy from 578 patients and about the number of biopsies from 516 patients. In 91% the biopsy led to the diagnosis of a cancer. In 9% the biopsy was false-negative. An accuracy of nearly 100% was achieved in biopsies of erosive or ulcerating lesions (Types IIc or III). The main part of false negative biopsis originated from mucosal lesions without mucosal defect. The higher the number of biopsy particles from one lesion, the higher the bioptic accuracy, and it is proportionally increasing up to 12 biopsies for one lesion. In several cases, more biopsies than 12 were needed.

Table 5. Gastrointestinal hemorrhage as first symptoms of E.G.C.

Age	Total E.G.C.	Hematemesis and Melena ($n = 649$)
0–20	1	–
20–29	9	1
30–39	42	2
40–49	103	14
50–59	151	12
60–69	200	28
70–79	131	13
80–89	11	3
90–99	1	–
		Total 73 (11.2%)

Table 6. Results of biopsy I ($n = 578$)

Biopsy positive	525 (91%)
Biopsy false-negative	53 (9%)

Table 7. Results of biopsy II ($n = 516$) (1–9 or more biopsies were taken from 516 E.G.C.)

Number of biopsies	False-negative biopsies
1–4 189 ×	22 × 12%
5–8 212 ×	17 × 8%
9 and more 115 ×	4 × 3.4%

Cytology

159 patients ($n = 658$) have had cytologic examinations. In 115 (72%) malignant cells could be found. In the 53 patients with a false-negative biopsy, a cancer could be detected in 18 cases by cytology. Of the examiners 26% used the washing-out method for cytology, 58% the brush method and 16% combined both methods. One examiner completed the histologic examination by a cytologic judgement of the biopsy particle and another examiner had done enzyme determination in biopsy particles.

Discussion

The age adjusted death rate of gastric cancer in Japan [1] (61.62 for men and 32.62 for women) is 2 or 3 times higher than in most countries of Europe (Table 1).

In a specialized Japanese clinic (Tokyo Women's Medical College) (Table 8) 1 E.G.C. is found in 67 gastroscopies which is 4.5 times more than the European average (1:308 for the 10-year-period 1968–1977), but only 1.8 to 3 times higher than in some European centers (Table 8). If we consider the much lower incidence of gastric cancer in Europe compared to Japan, these ratios prove that the European endoscopists have learned to recognize the early stages of gastric cancer and that some of us are doing their job as well as our Japanese colleagues. But there are great differences between one examiner to another (Table 8) and from country to country (Table 1).

Table 8. This table shows the results of some important endoscopic centers in Europe during the period 1973–1977. The code-number corresponds to the number of our own registration. X-ray examination: These figures indicate in how many cases a suspected X-ray finding led to endoscopy

Country	Code-Number of Examiner	Total Scopies	Total CA	% CA	Total E.C.	Percentage EC/CA	Ratio EC/ Scopies	X-ray-Examinations
J	1	15, 114			225		1: 67	
CH	55	1, 660	72	4,3%	16	22.2%	1:104	23%
A	202	2, 548	280	11%	19	6.78%	1:134	63%
USSR	132	3, 732	98	2.6%	22	22.4%	1:170	0%
A	47	4, 449	142	3.19%	29	20.4%	1:153	13.8%
D	169	9, 498	445	4.7%	36	8.1%	1:264	36%
CH	266	2, 668	69	2.5%	10	14.5%	1:267	66%
D	16	10, 050	274	2.7%	37	13.5%	1:272	40.5%
YU	133	12, 124	574	4.7%	38	6.6%	1:319	0%
D	178[a]	6, 439	162	2.5%	20	12.3%	1:322	5%
F	158	3, 800[b]	49	1.28%	31	63.3%	1:123	100%
		5, 700[c]	64	1.12%	7	10.9%	1:814	0%
F	256	17, 760	708	3.9%	39	5.5%	1:455	

[a] With Gastrocamera
[b] With previous X-ray examination
[c] Without previous X-ray examination

In analyzing the results of some endoscopic centers in Europe, we can see that those working additionally with gastrocamera do not achieve better results than those working with the scope only (Table 8).

It seems that the mass survey by standardized X-ray examination in Japan helps to detect a large number of E.G.C. In Europe, this fact is proven by the statistics of Prof. Paris and his coworkers in Lille (France), documented in his questionnaire sent to us: This group diagnosed 38 E.G.C between 9500 gastroscopies. In one section with 3800 gastroscopies, previously examined by X-ray, 31 E.G.C., or 1 E.G.C. to 123 gastroscopies were found. In a second group examined in urgency, without X-ray examination, only 7 E.G.C. were detected between 5700 gastroscopies, or 1 E.G.C. out of 814 gastroscopies. These figures, as well as those from different authors [3–7, 10, 18, 19, 21, 24) show clearly that the best results are obtained by combining a meticulous X-ray examination with a very well-done gastroscopy and with numerous biopsies. The accuracy of diagnosis is augmented proportionally with the number of biopsies.

Symptoms

Of all patients with an E.G.C. 94% have had complaints for several months or years (Table 4). This long period is compatible with the slow growth of an E.G.C. proven by Kawai [10a]. However, it must be pointed out that it is still not clear whether this percentage of complaints applies to all small gastric cancers, also to the nondiagnosed ones, or whether these remain largely asymptomatic. Symptoms in discovered E.G.C. may have been the real reason for check-up and diagnosis. On the other hand, Gutmann [7] is convinced that gastric cancer in its

early stage leads to uncharacteristic complaints, and he states that these cases must be considered a cancer until the diagnosis can be excluded.

The fact that in 11.7% of the patients over the age of 40 with an E.G.C. there was gastrointestinal bleeding, underlines the necessity of a very carefully done gastroscopy in every case of hematemesis and/or melena.

Location and Types of E.G.C.

Of E.G.C. 54.5% were located in the gastric angle, the antrum, and pylorus (Fig. I). Only 45.5% were found in the relatively greater extension of cardia, fundus, and corpus. Of E.G.C. 44% were located in the so-called Magenstraße, a region of small extension, too. Angulus, antrum, pylorus, and Magenstraße therefore may be considered as zones of predilection.

Types IIa nd IIb are the rarest ones with 11.53%, followed by Type I (21%), Type III (26,5%). Type IIc was the most frequent one with 29.5%.

The distribution of the different types seems to be uniform all over the stomach.

The percentage of E.G.C. of all diagnosed gastric cancers is still small (6.2%). However, in very active and well-trained centers, the percentage of E.G.C. between all resected gastric carcinoma is increasing (VIII). Searching E.G.C. remains a fruitful objective. The answers of three contacted institutes of pathology show it clearly: The percentage of all gastric cancers was 21% in *Hamburg-Eppendorf* (D. Mitschke, Univ.-Krankenhaus Eppendorf, Pathologisches Institut Hamburg), 15% in *Erlangen* (P. Hermanek, Abt. für klinische Pathologie, Chirurgische Klinik, Universität Erlangen-Nürnberg), and 9.2% in *Munich* (M. Eder, Pathologisches Institut, Universität München).

References

 1. Cancer Facts and Figures, 1977 (American Cancer Society), p. 15
 2. Elster, K.: Personal communication, 1978
 3. Frik, W.: Early Radiologic Diagnostics of Stomach Cancer. Early Gastric Cancer. Berlin, Heidelberg, New York: Springer 1974, 76–81
 4. Gutmann, R. A.: De quelques signes radiologiques du cancer gastrique au début. Bull. Soc. Méd. Franc. **21**, 347–351 (1933)
 5. Gutmann, R. A.: Le diagnostique précoce du cancer gastrique. 2. Intern. Gastroenterologie Kongress, Paris, 1937
 6. Gutmann, R. A., Bertrand, I., Peristiany, J.: Le cancer de l'estomac au début. G. Doin, Paris, 1939
 7. Gutmann, R. A.: Le diagnostique du cancer précoce de l'estomac à la période utile. G. Doin, Paris, 1956
 8. Hayashida, T.: Prognosis of the resected early gastric cancer. Jap. Gastroent. Endoscopy (Tokyo) **11**, 1969, 115
 9. Kapany, N. S.: Endoscopes using Fiber Optics. Proceedings of the International Congress of Gastroenterology, Leyden, Noorwiyk aan Zee, 577–584 (1960)
10. Kawai, K., Tanaka, H.: Differential Diagnosis of Gastric Diseases. Igaku Shoin Ltd. Tokyo, 1974
10a Kawai, K., Miyaoka, T., Kohli, Y.: Evaluation of Early Gastric Cancer from the Clinical Point of View. Early Gastric Cancer. Berlin, Heidelberg, New York: Springer 1974, 63–66

11. Kidokoro, T.: Frequency of Resection, Metastasis on Five-Year Survival Rate of Gastric Carcinoma in a Surgical Clinic. Gann Monograph on Cancer Research, Vol. 11, Baltimore, London, Tokyo: University Park Press 1972, 45
12. Konjetzny, G. E.: Zur Frage der Frühdiagnose und Prophylaxe des Magenkrebses. Med. Klinik, 1935
13. Konjetzny, G. E.: Zur Frühdiagnose des Magenkrebses. 2. International Congress for Gastroenterology. Paris 1937
14. Konjetzny, G. E.: Der Magenkrebs. Stuttgart: F. Enke 1938
15. Kurokowa, T., Kajitani, T., Oota, K.: Carcinoma of the Stomach in Early Phase. Nakayama-Shoten, Tokyo, 1967
16. Miller, G., Kaufmann, M.: Das Magenfrühkarzinom in Europa – 1170 Fälle aus den Jahren 1968–1973. Dtsch. med. Wschr. **100**, (1975) **39** (1946–1949)
17. Nakamura, K.: Pathohistological examination. In: Kurokawa, T., Kajitani, T., Oota, K. (ed.), Carcinoma of the Stomach in Early Phase. Tokyo: Nakayama-Shoten 1967
18. Shirakabe, H.: Das Frühkarzinom des Magens. Stuttgart: Thieme 1969
19. Shirakabe, H.: Double Contrast Studies of the Stomach. Stuttgart: Georg Thieme Verlag, 1972
20. Tasaka, S.: Statistical Study of Early Gastric Cancer, collected throughout Japan. Gastroenterol. Endoscopy (Tokyo) **4** (1962)
21. Treichel, J., Oeser, H.: Die Doppelkontrastmethode: Optimale Technik der röntgenologischen Magenuntersuchungen. Dtsch. med. Wschr. **100**, 2226–2229 (1975)
22. Uji, T.: zitiert nach H. Oshima: "Gastrokamera" in der Diagnostik von Magenerkrankungen. In: F. Holle: Spezielle Magenchirurgie, S. 129. Berlin, Heidelberg, New York: Springer 1968
23. Versé, M.: Über die Entstehung, den Bau und das Wachstum der Polypen, Adenome und Karzinome des Magendarmkanals. Arb. Path. Inst. Leipzig **1**, 1908, 40–74
24. Yamagata, S., Masuda, H.: Magenkarzinom. In: Klinische Gastroenterologie I. L. Demling (ed.). Stuttgart: Thieme 1973, 237–249