

Evaluation of specific value of endoscopic biopsies and brush cytology for malignancies of the oesophagus and stomach

L. WITZEL, F. HALTER¹, P. A. GRÉTILLAT, U. SCHEURER, AND M. KELLER

From the Gastrointestinal Unit and Institute of Pathology, University of Berne, Berne, Switzerland

SUMMARY The value of multiple biopsies and brush cytology at oesophago-gastroscopy was assessed in relation to macroscopy and localization on 100 verified tumours in a prospective study. The cumulative accuracy achieved was 96%. This was significantly better ($P < 0.01$) than that of biopsy (83%) and of cytology (85%). While the reliability of both procedures was not significantly different in malignancies of the oesophagus, the gastric body, and the antrum, cytology was significantly more accurate in cancers of the cardia (90% and 55% respectively, $P < 0.05$). Cytology was also more reliable in stenosing tumours (92%/72%, $P < 0.05$). In polypoid malignancies a positive but not significant trend was found in favour of multiple biopsies (94%/64%). One of the two early cancers was only diagnosed by cytology. The results confirm the high diagnostic accuracy of multiple endoscopic biopsies combined with brush cytology and demonstrate the value of cytology in stenosing tumours, especially in those of the cardia.

The reported rate of accuracy of multiple endoscopic biopsies and of brush cytology is at great variance. False negative results were observed between 7% and 68% for biopsy (Dollinger, 1972; Hampel *et al.*, 1974) and 4.2%-56% for brush cytology (Kobayashi *et al.*, 1970; Dollinger, 1972). In the light of the difficulties in deciding whether an endoscopically visualized lesion is benign or malignant and the high value of a correct pre-operative diagnosis, it was considered to be important to assess the reliability of both procedures in a prospective study. Also little is known of the value of both procedures in relation to the macroscopic aspect and the localization of an individual lesion and this question was therefore included in the protocol.

Methods

Two hundred and fifty-one patients with endoscopically suspect oesophageal (58) and gastric (193) lesions were investigated. The age of the 167 male and 84 female patients varied between 22 and 88 years (mean 57.8 years). Thirty-one had two ex-

aminations, 27 had three, six had four, and three had five. The observations in the tables relate to the initial endoscopy only.

After an overnight fast and premedication with 5-10 mg diazepam intramuscularly, a fiberoptic gastroduodenoscope type ACMI FO-7089 P or Olympus GIF0₂ was introduced. The lesion was first biopsied and six to 10 tissue samples were taken using the standard biopsy forceps. The material was immediately fixed in 4% formaldehyde.

A standard type Olympus or ACMI cytology brush was then introduced through the biopsy channel of the instrument and the total area of the lesion was vigorously brushed. The brush was removed and the tip rinsed in approximately 10 ml saline. This suspension was centrifuged within two to three hours after sampling at 3000 rpm for 10 minutes. The sediments were distributed on slides, fixed with Delaunay solution and stained according to the Papanicolaou technique. Biopsy material and cytology specimens were examined in two independent laboratories by different investigators.

According to the macroscopic assessment and the subjective impression of four experienced investigators, the lesions were graded in five categories: (1) suspicion very low, (2) suspect, and (3) very suspect lesions, (4) definitely malignant lesions, and (5) no differentiation possible.

¹Address for correspondence: Dr F. Halter, Gastroenterologische Abteilung, Inselspital, 3010 Berne, Switzerland.

	Total	Operation	Necropsy	Follow-up		Biopsy from metastases	No follow-up
				Endoscopic	Clinical		
Carcinoma							
Oesophageal	27	6	1		18	2	0
Gastric	70	58	3		6	3	0
Gastric sarcoma	3	2	1				
Gastric ulcer	95	32	2	49			12
Reflux oesophagitis	31	7	1	19			4
Atypical gastric fold	11			7	1		3
Erosion	6			3			3
Scar	4			2			2
Operated stomach	4			4			
Total	251	105	8	84	25	5	24

Table 1 Final diagnosis in 251 patients suffering from oesophageal (58) and gastric (193) lesions

Results

The final diagnosis of the lesions found at endoscopy are summarized in Table 1. Furthermore, information is given on how the diagnosis was verified. Twenty-seven of 100 tumours—97 carcinomas, three sarcomas—were localized in the oesophagus, 20 at the cardia, 26 in the gastric body, 21 in the antrum, and six within an operated stomach (Table 2). Eighty-three were verified by multiple biopsies, 85 by brush cytology. The cumulative accuracy reached 96%, and was significantly better than that of either procedure alone ($P < 0.01$, χ^2 test). Both histology and cytology were negative in one oesophageal tumour and three carcinomas of the gastric body. In tumours of the cardia, the accuracy of the biopsy results was significantly smaller than that of cytology (55%/90%, $P < 0.05$, χ^2 test). In all the other localizations the differences between the yield of either technique were not significantly different.

	Total	MB	BC	MB + BC	Failure
Oesophagus	27	25	24	26	1
Cardia	20	11	18	20	
Body and fundus	26	21	20	23	3
Antrum	21	20	17	21	
Recurrences in operated stomach	6	6	6	6	
Total	100	83	85	96	4

Table 2 Diagnostic accuracy of multiple biopsies (MB) and brush cytology (BC) in 100 verified malignancies according to localization

An analysis of the data in respect of macroscopy (Table 3) gives significantly better results from cytology in 39 stenosing tumours with a diagnostic accuracy of 92% as compared with 72% for biopsy ($P < 0.05$, χ^2 test). In the 17 polypoid tumours, there was a positive trend in favour of the biopsy (diag-

	Total	MB	BC	Failure
Stenosing	39	28	36	1
Tumourous ulcerated	26	26	23	
Polypoid tumourous	17	16	11	
Ulcerated	12	9	10	2
Elevated	3	2	2	1
Scar, erosion	3	2	3	
Total	100	83	85	4

Table 3 Diagnostic accuracy of multiple biopsies (MB) and brush cytology (BC) in 100 verified malignancies tabulated according to growth

Endoscopic appearance	Final diagnosis			
	Benign (no.) (%)	Benign (%)	Malignant (no.) (%)	Malignant (%)
No differentiation	8	6.3	4	4
Suspicion very low	79	62.2	6	6
Lesion				
Suspect	27	21.3	6	6
Very suspect	13	10.2	64	64
Malignant	0	0	20	20
Total	127	100	100	100

Table 4 Endoscopic appearance correlated with final diagnosis

nostic yield 94% as compared with 64%), but the difference was not significant ($P < 0.1$, χ^2 test).

In Table 4, the endoscopic aspect is correlated with the final diagnosis; 10.2% of those with a high suspicion were benign lesions. On the other hand, 12% with very low or low suspicion were malignant. In one out of the two early cancers only cytology was positive. In two ulcerative tumours with a positive cytology malignancy was not verified; however, in one of the two a complete histological examination of the operative specimen was not possible due to a technical error.

Discussion

The results of this study underline that a reliable classification of endoscopically visualized findings is

not possible on the macroscopic aspect in a considerable proportion of eosophago-gastric lesions. An adequate diagnosis is, however, of vital importance in small tumours, especially in the non-invasive, so-called early cancers. Two such lesions observed in this study were not diagnosed as malignancies and were classified macroscopically as benign ulceration and erosion respectively.

The 83% diagnostic yield of multiple biopsies matches well with that of other series and demonstrates the high accuracy that can be achieved by endoscopic biopsy in modern fiberoptic endoscopy. In a review of 11 authors, seven had a diagnostic accuracy between 84% and 92% for biopsy and the average value for this method was 87% (Hermanek, 1973). The data show, however, that additional and significantly better information can be gained by combining biopsy sampling with brush cytology. One of the two early carcinomas was identified only by brush cytology. In stenosing tumours, especially in those of the cardia, the diagnostic accuracy of brush cytology is significantly higher than that of multiple biopsies. This simple technique neither prolongs examinations significantly nor does it increase the risk of the procedure. Until now, there have been no reports of complications of brush cytology (Witte, 1972). The diagnostic yield of cytology certainly depends on the skill of the examiner but, in addition, the sampling technique and the processing of the material are of the utmost importance. Lavage cytology is a time-consuming and less accurate procedure and the extra information gained with this technique in our hands was not significant (Witzel *et al.*, 1974). The incidence of

false positive results varies in the literature from 0.25-6.5% (Prolla *et al.*, 1972; Rachail *et al.*, 1974; Weidenhiller, 1974). It is small in this study and it should be remembered that a negative finding in an operative specimen does not exclude an early carcinoma unless the material is subjected to a very detailed analysis.

References

- Dollinger, H. (1972). Zur endoskopischen Beurteilung neoplastischer Wandveränderungen an Ösophagus und Magen. *Leber Magen Darm*, **2**, 139-141.
- Hampel, K. E., Stopik, D., and Niedobitek, F. (1974). Der diagnostische Wert von gezielten Biopsien bei Magentumoren. *Zeitschrift für Gastroenterologie*, **12**, 315-320.
- Hermanek, P. (1973). Gastrobiopsy in cancer of the stomach. *Endoscopy*, **5**, 144-147.
- Kobayashi, S., Prolla, J. C., and Kirsner, J. B. (1970). Brushing cytology of the esophagus and stomach under direct vision by fiberscopes. *Acta Cytologica*, **14**, 219-223.
- Prolla, J. C., Xavier, R. G., and Kirsner, J. B. (1972). Exfoliative cytology in gastric ulcer. Its role in differentiation of benign and malignant ulcers. *Gastroenterology*, **16**, 33-37.
- Rachail, M., Rachail-Arnoux, M., Colomb, M., and Mouriquand, C. (1974). Le cytodagnostic gastrique et oesophagien sous controle endoscopique. *Lyon Médical*, **231**, 325-332.
- Weidenhiller, S. (1974). Gastroenterologische Zytodiagnostik. *Deutsche Medizinische Wochenschrift*, **99**, 8-11.
- Witte, S. (1972). Die zytologische Tumordiagnostik. *Fortschritte der Medizin*, **90**, 366-368.
- Witzel, L., Halter, F., Grétilat, P. A., Scheurer, U., Wanger, F., and Blank, H. R. (1974). *Diagnostische Wertigkeit von Biopsie, Bürsten- und Spülzytologie bei endoskopischem Verdacht auf maligne Oesophagusoder Magenaffektionen*. Presented at the annual meeting of the Schweizerische Gesellschaft für Gastroenterologie, Freiburg, September 19-21.