

Curative management of adenocarcinoma of the esophagus

Endoscopic treatment

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Background

The incidence of adenocarcinoma of the esophagus has increased continuously during the last decades. Chronic acid reflux is strongly associated with adenocarcinoma of the esophagus and is the main cause of the development of specialised intestinal metaplasia in the esophagus (Barrett's esophagus). Barrett's esophagus is therefore considered a precancerous condition. Published data on malignant transformation in Barrett's esophagus show rates varying between 1 in 46 and 1 in 141 patients / years. More recent prospective data show that in Barrett's esophagus with histologically proven severe dysplasia adenocarcinoma subsequently develops in up to 34%.

The treatment of choice with curative intent has been esophagectomy. However, even at surgical centres that have sufficient experience and even, when patients are selected carefully, the mortality rates are in the range of 3% and 5% with Barrett's early carcinoma (EC) and high-grade dysplasia (HGD), respectively. There is a significant morbidity rate ranging from 18% to 48%. In view of these facts and because of the relatively large proportion of patients, who are unable to undergo surgery because of comorbidity or age, the question arises whether local endoscopic therapy might also be applicable in Barrett's EC and HGD, in analogy with early gastric cancer. Arguments in favour of intraluminal treatment by means of endoscopic techniques are as follows: morbidity and mortality should be essentially lower than in esophagectomy. With endoscopic techniques there is no mayor loss of quality of live. Furthermore, there are no risks for lymph node metastases in proven HGD and the risk for lymph nodes metastases is almost zero in patients with mucosal Barrett's cancer. Preliminary data negate, that in analogy to early gastric cancer, the lymph node metastases risk is a very low, too (probably 1-2%) in patients with Barrett's carcinoma from the submucosa level-type (SM 1 cancer). However, the lymph node metastases rate ranges between 10 and 20% in submucosal cancer of the 2nd and 3rd level (SM 2 and SM 3 cancer).

Staging procedures

In consequence, carefully designed staging procedures are necessary to find-out preoperatively the

patients with low risk for lymph node metastases, if local endoscopic treatment is scheduled. The staging procedures include — at least in our specialised centre — high-resolution video endoscopy with mapping biopsies, chromoendoscopy with methylen blue and biopsies of unstained or discoloured lesions. A standard endosonography with 7.5 to 12 mHz is performed to detect lymph node enlargements in the mediastinum and the truncus coeliacus. In addition, a mini-endosonography through the scope with probes of 20 mHz can be performed to investigate the infiltration depth of the tumour.

Abdominal ultrasound and spiral computerized tomography of the thorax / mediastinum and the upper abdomen are oncological standards.

In some cases additional endoscopic mucosal resection is used for diagnostic purposes to get a clear information about the infiltration depth. Drug-induced or auto-fluorescence endoscopy are still experimental diagnostic methods.

The aims of the staging procedures are the exact mapping of the whole Barrett's segment; that means, detection of synchronous lesions, measurement of the diameter of the malignant lesion and furthermore description of the tumour surface as a polypoid (type I), flat (type II a, b, c) or ulcerated (type III). Concerning the infiltration depth we want to differentiate between mucosal type, submucosal type I, submucosal type II and III and, finally T2 tumours. Another important aim of the staging procedure is to get information about the tumour grading (G1-G3).

In analogy to early gastric cancer we hope to define "low-risk Barrett's carcinoma" and HGD as follows: uni-ocular lesions smaller than 2 cm, surface type I or II, infiltration type M or SM I, grading type G1 or G2 and lymph status negative.

Endoscopic treatment techniques

Three main endoscopic treatment techniques are available: endoscopic mucosal resection (EMR), photodynamic therapy (PDT) and thermoablation techniques as lasers and electrocoagulation. Details of the different treatment options can be obtained by the cited literature at the end of the manuscript.

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Since all the treatment modalities have advantages and disadvantages (see literature), one should use a differentiated choice of the local treatment. Actually, we are using the EMR in about 60%, the PDT in about 30% and both, PDT in combination with EMR, in about 10%. Thermal methods should only be used for optimising the local endoscopic treatment and not as initial treatment.

Results

Actually there are only few published data on local endoscopic therapies of Barrett's EC and HGD. Besides of some small casuistic series, there are only two groups with larger experiences: The Overholt group in USA reported on 100 patients with mainly high-grade dysplasia (> 70% HGD), treated exclusively by photodynamic therapy with hematoporphyrine derivates as photosensitizer. They achieved a local remission rate of about 80%, however, the rate of major complications was 34% and consisted of strictures of the esophagus which had to be treated by repeated dilation. In 1998 our own group reported about 32 patients with HGD and EC using aminolevulinic acid. Due to the high concentration of the photosensitizer only in the mucosa and the short retention time in the body, severe side effects were never observed. However, the tumour destruction by this kind of PDT is limited to a maximum of 2 mm tissue depth. This circumstance was reflected by the results: we achieved a 100% complete remission rate in HGD but only 75% complete remission rate in EC. In the meantime we gathered experience with 70 patients altogether, treated by PDT (results not yet published). This year our group will publish a larger experience in endoscopic mucosal resection. Prospective Investigation of EMR was conducted in 64 patients (61 patients with EC and 3 patients with HGD). 35 patients met the criteria for low risk. A total of 120 EMR was performed with only 1 major complication. A spurting bleeding could be managed endoscopically. Complete local remission was achieved significantly earlier in the low-risk group than in the high-risk group. A complete remission was achieved in 97% (34/35) of the patients in the low-risk

group. In the high-risk group the complete remission rate was lower (59%). However, life table analyses showed that in this group a similar complete remission rate can also be expected after completion of all therapeutic steps.

Updated results of 114 out of 157 patients, who were treated locally in our center within the last 3 years (10/1996-9/1999) showed a complete remission rate of 98%.

Only 2 patients were treatment failures and were treated by esophagectomy. The rate of major complications was 7%. During the follow-up of 18 months (mean) in 26 patients metachronous lesions were detected and treated by endoluminal techniques again (the results are not yet published).

Conclusions

Without any doubt radical surgical resection is still the treatment of choice for superficial Barrett's EC and HGD. Local endoscopic methods or intraluminal therapy are still experimental. However, the concept of local treatment is attractive because of the low morbidity, low mortality and the preservation of quality of life. The data currently available for intraluminal surgery show an excellent intermediate complete remission rate of more than 95%. However, long-term results have to be expected until esophagectomy will become the method of reserve.

References

1. GOSSNER L., STOLTE M., SROKA R., RICK K., MAY A., HAHN E.G., ELL C. Photodynamic ablation of high-grade dysplasia and early cancer in Barrett's esophagus by means of 5-aminolevulinic acid. *Gastroenterol.*, 1998, **114**: 448-455.
2. GOSSNER L., MAY A., STOLTE M., SEITZ G., HAHN E.G., ELL C. KTP laser destruction of dysplasia and early cancer in columnar-lined Barrett's esophagus. *Gastrointest. Endosc.*, 1999, **49**: 8-12.
3. ELL C., MAY A., GOSSNER L., PECH O., GÜNTHER E., MAYER G., HENRICH R., VIETH M., MÜLLER H., SELTZ G., STOLTE M. Endoscopic Mucosal Resection of Early Cancer and High-Grade Dysplasia in Barrett's Esophagus. *Gastroenterol.*, 2000, **118**: 1-9.