

ABSTRACT

Introduction: Esophageal cancer ranks eighth among the most common malignancies worldwide. The two most common types are adenocarcinoma and spinocellular carcinoma. Correct histopathological diagnosis, cancer staging and identification of predictive risk factors of progression are important in terms of further disease course and management. While patients with mucosal carcinoma without risk factors are treated endoscopically, those with submucosal invasion or mucosal carcinoma with risk factors are referred for surgical therapy according to current recommendations. Histopathology is still considered the gold standard in diagnosis, often used in conjunction with immunohistochemistry, e.g., to document a TP53 gene mutation, which plays an important role in the pathogenesis and progression of esophageal dysplasia. New diagnostic methods, such as confocal laser endomicroscopy (CLE), also play an important role. Other crucial factors include patient follow-up, early and reliable detection of persistent or recurrent lesions.

Aims, methods and patients: In the thesis, 4 separate, partly connected projects are assessed together, with a partial overlap of patients. The aims of the individual projects were as follows: 1) To identify predictive factors of esophageal cancer progression, risk of metastasis and generalization, and to compare the effectiveness of endoscopic and surgical therapies in 65 patients with "high-risk" early esophageal cancer. 2) p53 as an immunohistochemical marker and its significance were investigated in 87 patients with esophageal lesions. 3) The diagnostic accuracy of standard biopsies and CLE was compared in 65 patients with 74 visible esophageal/gastric lesions. 4) To compare CLE with biopsies in the detection of persistent/recurrent intestinal metaplasia and neoplasia in 56 patients.

Results: 1) The only statistically significant prognostic factor of generalization and lymph node metastasis was documented blood or lymphatic vessel invasion. A total of 80 % of endoscopically treated patients achieved complete endoluminal remission. Long-term remission was achieved in 62.9 % of patients. 2) p53 immunohistochemistry was diagnostic in 73 % of dysplastic lesions and 100 % of adenocarcinoma showed an abnormal phenotype. 3) Diagnostic accuracy to confirm or exclude a malignant lesion was 85 % for biopsies and 89 % for CLE. 4) Biopsies detected intestinal metaplasia after endoscopic therapy in 94.6 % and CLE in 100 %. Diagnostic agreement between CLE and biopsies was 94.6 %.

Conclusions: 1) Cancer invasion into lymphatic and blood vessels appears to be the most significant risk factor predicting esophageal cancer progression. Patients with mucosal carcinoma without risk factors or with carcinoma invading the upper third of the submucosa could be treated endoscopically, and the criteria limit could be shifted in these indications. 2) Immunohistochemical detection of p53 is a suitable auxiliary method, especially in differentiating dysplastic and nondysplastic esophageal

lesions. 3) CLE is comparable to standard biopsies in overall diagnostic accuracy in esophageal and gastric lesions and could be recognized as a standard method in this indication. 4) The accuracy of CLE in diagnosing persistent/recurrent intestinal metaplasia and in excluding recurrent neoplasia is comparable to that of standard biopsy.

Compared to biopsy, the advantage of CLE in both indications (3rd, 4th) is examination of a significantly larger area and real-time evaluation during endoscopy even by a trained gastroenterologist without the participation of a pathologist.

Key words: esophageal cancer, high-risk cancer, endoscopic therapy, confocal laser endomicroscopy, CLE, p53