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Minimally Invasive Esophagectomy for Barrett's with High-grade Dysplasia and Early Adenocarcinoma of the Esophagus

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There has been a dramatic increase in the incidence of esophageal cancer in the Western population over the last two to three decades.¹ Further, the pattern of esophageal cancer has changed, with an increase in the incidence of adenocarcinoma, while the incidence of squamous cell carcinomas has declined. The reason for this increase is not clear, but gastroesophageal reflux disease, obesity, and Barrett's esophagus have been identified as risk factors.² High-grade dysplasia (HGD) in Barrett's esophagus is a premalignant condition which can progress to invasive adenocarcinoma. We have previously reviewed the important issues with regard to the treatment of HGD and early cancer.^{2,3}

In this paper, we summarize some of the important aspects of HGD, the incidence of adenocarcinoma in resected specimens, issues regarding the clinical behavior of T1 adenocarcinomas, and the surgical aspects in the treatment of HGD and early-stage adenocarcinoma (T1) with a particular focus on minimally invasive esophagectomy (MIE).

High-grade Dysplasia

High-grade dysplasia is defined as intraepithelial neoplasia that has not yet penetrated the basement membrane and represents the final step in the metaplasia–dysplasia–carcinoma sequence in the transformation of Barrett's esophagus to adenocarcinoma.⁴ The optimal approach to the treatment of HGD is controversial.

There are relatively few studies which address the rate of progression of HGD to adenocarcinoma.^{2,5–7} In one study, Reid and colleagues reported a 59% 5-year cumulative

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risk of cancer among 76 patients with HGD.⁶ In addition, there are difficulties in the diagnosis of HGD. First, there are sampling errors in the diagnosis of HGD and early neoplasia. Cameron mapped the esophagectomy specimens in patients with HGD and detected areas of microscopic carcinoma, which were frequently small (<1.1 cm²).⁸ Thus, even with a vigorous biopsy protocol, carcinomas can be missed.

Further, pathologists differ on their opinion as to whether or not HGD is present, and interobserver disagreement among experienced pathologists for the differentiation of HGD versus intramucosal carcinoma is significant.⁹ In a study by Ornsby and colleagues, the interobserver agreement among pathologists was only fair and did not improve with establishment of standard criteria.^{2,10}

Occult Adenocarcinoma in Patients with HGD

Surgical series evaluating the incidence of occult adenocarcinoma in patients who had undergone an esophagectomy for HGD show an incidence of up to 75%.² Pelligrini and Collard have summarized several series of patients who underwent esophagectomy for high-grade dysplasia.^{11,12} We have also presented an update of several series comprising 371 patients, with the incidence of occult carcinoma being 42%.²

Some of the drawbacks of these studies are that they are retrospective and do not define the endoscopy protocol followed prior to the diagnosis of HGD. Nevertheless, the incidence of missed adenocarcinoma in these patients is very high, despite an intensive biopsy protocol.² Therefore, because the detection of invasive adenocarcinoma in the resected specimens of patients with a pre-resection diagnosis of HGD being very high, one can make a strong argument for esophagectomy in fit patients.²

Korst and Altorki summarized the findings in 140 patients who underwent esophagectomy for HGD, 59 (42%) of those had adenocarcinoma in the resected specimen. Of these patients, 43 had T1 lesions, nine had T2 lesions, and six had T3 lesions. Thus, in 25.4% of patients with invasive cancer, the tumors invaded beyond the muscularis propria.⁴ Thus, mucosal ablation therapy alone is inadequate to treat a significant percentage of these patients.

Impact of Earlier Diagnosis and Survival After Esophagectomy

Esophageal cancer, when diagnosed, has an overall 5-year survival of approximately 10–15%.¹ The main reason for this poor prognosis is the advanced stage at diagnosis. In contrast, patients who are diagnosed early and have surgical resection have a good prognosis. For example, the 5-year survival among patients with Stage 0 lesions (tumor in situ) is greater than 95% and in Stage 1 patients is 50–80%. Thus, treatment at an earlier stage is associated with a better outcome.^{1,2} Surgical intervention via esophagectomy in patients with HGD, many of whom may be harboring early invasive cancer, or early-stage T1 lesions, offers the best chance for cure in fit patients.

The Role for Esophagectomy in HGD and T1 Esophageal Cancer

Esophagectomy offers the most definite treatment in that it eliminates all of the Barrett's epithelium and the mucosa at risk. On the other hand, critics point out that the morbidity and mortality has been considered high¹³ and many of these patients may not harbor cancer at the time of resection. One of the main concerns for recommendation of esophagectomy is the risks associated with surgery. Certainly, one of the most important factors in lowering the risk of esophagectomy is the experience of the surgeon doing the esophagectomy. In an effort to decrease the morbidity and mortality from this surgery, recent advances in

minimally invasive surgery have allowed us to develop and refine the technique of minimally invasive esophagectomy at the University of Pittsburgh.

We have reported our results of a series of 222 consecutive MIEs.¹⁴ The median ICU stay was 1 day, the hospital stay 7 days and the operative mortality was only 1.4%. In addition, stage-specific survival was similar to open esophagectomy series. Thus, in our center, we observed a short hospital stay, low mortality, and good oncologic results after MIE.

Esophagectomy for T1 Esophageal Cancer

T1 esophageal cancers encompass a very heterogeneous group of patients. This heterogeneity includes not only depth of the tumor (intramucosal or submucosal) but also other prognostic factors such as the length of the tumor, the presence of angiolymphatic invasion, nodal metastases, and the degree of differentiation, even in these superficial tumors. Although, it is commonly stated that patients with T1 intramucosal cancer can be managed with endoscopic therapies, due to the lower chance of lymph node metastases, these associated factors may in fact preclude adequate treatment with endoscopic therapies.³

We recently reported our experience in 100 consecutive patients who underwent esophagectomy for T1 esophageal carcinoma. A minimally invasive approach was used in 80% of the patients.³ This series included all patients with T1 tumors, including those with adverse prognostic factors. In our study, the 30-day mortality was zero. The resection margins were microscopically negative in 99% (99/100) of patients. N1 disease was present in 21 patients [T1a:2/29 (7%); T1b:19/71 (27%)], associated high-grade dysplasia in 64/100 (64%) and angiolymphatic invasion in 19/100 (19%) patients. At a median follow-up of 66 months, the estimated 3 year disease-free survival for all patients (including N1) was 80%. Nodal status and size/length were significantly associated with overall survival and disease-free survival, respectively. Patients with T1 cancer have the best chance for cure and esophagectomy can be performed safely in these patients in experienced centers.³

Quality of Life

With advances made in surgical techniques, and perioperative surgical critical care, the mortality and morbidity from esophagectomy have decreased.² However, the long term quality of life (QOL) after esophagectomy is being increasingly recognized as an important factor. Despite potential problems, such as dysphagia, or dumping that may be associated with esophagectomy, studies suggest that the long-term impact on the QOL is minimal.^{2,3,14,15} In an effort to decrease the morbidity and preserve the QOL, we have adopted a minimally invasive approach. In one of our studies on outcomes after MIE, the general QOL was assessed by the Short-Form 36. There was no significant differences when the preoperative and post-operative scores were compared, indicating preservation of QOL. In addition, the reflux-related QOL was evaluated with the Gastroesophageal Reflux Disease-Health Related Quality of Life (HRQOL). The range of this score varies from 0 (no symptoms) to 45 (most severe symptoms). The mean HRQOL score was 4.6 indicating a normal score. Further, the dysphagia scores were excellent with a mean score of 1.4 using a scale of 1 (no dysphagia) to 5 (severe dysphagia). More recently, we evaluated the QOL in patients who undergone an esophagectomy for T1 esophageal cancer.³ At a mean follow-up of 48.2 months, the median HRQOL score was 3. Thus the QOL after minimally invasive esophagectomy appears to be well preserved.

Conclusion

In summary, the management of HGD is controversial. There is a significant risk of occult invasive cancer being already present or subsequently developing in patients with HGD.^{2,16}

Many patients with T1 esophageal cancer have several risk factors which may preclude adequate treatment with endoscopic therapy. Esophagectomy can be performed safely in patients with T1 cancer, with good long-term results.³ Esophagectomy should entail removal of all of the Barrett's mucosa and the anastomosis is commonly performed in the high chest or in the neck. Strong consideration should be given for the performance of surgery in a high-volume hospital. With esophagectomy for early-stage esophageal cancer, the long-term survival is excellent and these patients have a good quality of life.^{2,3}

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