Transhiatal oesophagectomy: treatment of choice for high-grade dysplasia

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Abstract

Objective: To demonstrate that transhiatal oesophagectomy should remain the gold standard treatment for patients with high-grade dysplasia.

Background: The conventional management of high-grade dysplasia of the oesophagus is surgery. Perceived high incidence of operative morbidity and mortality associated with oesophagectomy has led some to advocate alternative less invasive treatments such as endoscopic mucosal resection (EMR) and photodynamic therapy (PDT). We present our data on the use of transhiatal oesophagectomy for the management of high-grade dysplasia.

Methods: Twenty-three patients underwent transhiatal oesophagectomy for biopsy-proven high-grade dysplasia in a high volume centre, between March 2000 and December 2006. Twenty-two were male and 1 female with a mean age of 63.5 years (±6.5). Staging was ascertained by gastroscopy, EUS and CT. Two patients had PET CT. ASA grade was I (2), II (14), III (6) and IV (1). Results: Clinical anastomotic leak occurred in two patients (9%); this was managed conservatively. Four patients required intensive care admission. Occult adenocarcinoma was found in 35% (8/23) of surgical specimens; there were no involved nodes present. No re-operations were required. Median length of stay was 15 days (10—69). Thirty-day and in-hospital mortality was zero. There was one case of locally recurrent disease, and one death meaning that disease-free survival was 96%, and overall survival was 96% (22/23) at a mean follow-up of 35.4 months. Conclusions: Transhiatal oesophagectomy for high-grade dysplasia can be performed with acceptable mortality and morbidity when performed at a specialist centre.

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1. Introduction

Over the past 30 years, the incidence of oesophageal adenocarcinoma has increased markedly [1]. Adenocarcinoma has surpassed squamous cell carcinoma and now accounts for 70% of oesophageal cancer in the UK, where it is the fifth leading cause of cancer mortality [2]. Advanced disease has a poor prognosis [3] and hence in recent years treatment has been directed towards premalignant oesophageal lesions, in particular high-grade dysplasia (HGD), which when diagnosed confers a 40% risk of concomitant carcinoma in situ [4]. Studies have demonstrated that with adequate treatment, HGD in the absence of occult carcinoma confers a near 100% 5-year survival [5].

Differentiating between HGD alone and HGD with co-existent invasive adenocarcinoma is challenging and a subset of patients diagnosed with HGD at endoscopy is expected to have occult cancerous foci. This notion is supported by data from a number of studies which report that the incidence of occult adenocarcinoma in patients with HGD can range from 0% to 73% [4,6]. In spite of this, the treatment of HGD remains controversial. Though oesophagectomy is the only intervention to remove all the neoplastic tissue, perceived high incidence of operative morbidity and mortality associated with surgery has led some to advocate less invasive treatments such as endoscopic mucosal resection (EMR) [7] photodynamic therapy (PDT) [8] and endoscopic laser ablation [9].

We routinely perform transhiatal oesophagectomy (THO) for treatment of HGD, and in this study we report on results and outcomes in 23 patients with biopsy-proven HGD at a high volume tertiary centre.

2. Methods

Four-hundred and fifteen patients underwent oesophagectomy for cancer in our unit between March 2000 and December 2006. Twenty-three had a preoperative diagnosis of HGD and were treated with a transhiatal oesophagectomy. We retrospectively collected data on this cohort of patients. All patients underwent preoperative staging with endoscopic evaluation and computed tomography (CT). Endoscopic ultrasound (EUS) was performed on 18 patients and 2 had CT-PET scans. All were discussed at an upper GI multi disciplinary meeting (MDM) pre- and postoperatively. All 23 patients were operated under the supervision of one surgeon and underwent a transhiatal oesophagectomy with a sutured cervical oesophago-gastric anastomosis. A feeding jejunostomy was placed routinely. A pyloroplasty was not performed.
Postoperatively all patients were ventilated overnight in our recovery room and then transferred to the ward or high dependency unit depending on their clinical condition or comorbidities. On the third postoperative day a gastrograffin swallow was performed, which if normal lead to commencement of oral intake.

Follow-up was initially at 6 weeks from discharge and then subsequently 3 monthly for a year, 6 monthly for another 2 years, and then yearly. There were no cases of post-vagotomy dumping or gastro-oesophageal reflux on follow-up.

Diagnosis of high-grade dysplasia was confirmed by two independent consultant histopathologists, and was based on both architectural and cytological abnormalities. Architectural features deemed indicative of HGD are (1) a villiform or papillary surface, (2) crowding of glands with irregular branching and budding or (3) a cribriform architecture. Cytological features were (1) increased nuclear to cytoplasmic ratio with rounded or irregular nuclei with hyperchromasia and pleomorphism, (2) loss of polarity and nuclear stratification with loss of surface maturation as well as mucin depletion and (3) increased mitoses and atypical mitotic figures. These features would have to be identified by both histopathologists in order to make the diagnosis of HGD.

The following information was retrieved from case notes: age, sex, clinical presentation, preoperative staging, significant comorbidities, site and size of tumour, histopathological analyses pre- and post-resection, type of surgical procedure, intensive care stay, in-hospital stay, major and minor complications, anastomotic leak, development of local recurrence or distant metastases, last follow-up and cause of death.

3. Results

Of the 23 patients, 22 were male. The mean age was $63.5 \pm 6.5$ years at time of operation. Preoperative patient demographics and comorbidities are summarised in Table 1. All patients underwent a transhiatal oesophagectomy.

Four patients required intensive care postoperatively (17%). The median intensive care stay was 5.5 (3–7 days). The median hospital length of stay was 15 days (10–69 days). There was one intraoperative complication, which was an iatrogenic splenectomy.

No patient required a return to theatre. Postoperative complications were as follows: wound infection (5), chest infection (6), renal failure (2) anastomotic leak (3) anastomotic stricture (3) delayed gastric emptying (1). Of the three cases of anastomotic leak, one was radiological and two were clinical leaks. All were managed conservatively. Table 2 summarises the morbidities and mortalities associated with transhiatal oesophagectomy in this series.

Postoperative histology in 15 was HGD alone, while 8 specimens were found to have invasive adenocarcinoma (T1NO – 6, T2NO – 1, T3NO – 1). This data is summarised in Table 3. Positive longitudinal (1) and radial margins (1) were found in two of the specimens. The mean lymph node yield was 7 (0–19).

Thirty-day mortality in our series was zero, as was inhospital mortality. All 23 patients have been followed-up (median time of follow-up 35.2 months). One patient subsequently died following recurrence of disease at 21.3 months (stage T2N0M0, no lymphovascular invasion). To date, all 15 patients with HGD alone are alive.

4. Discussion

Intestinal metaplasia (Barrett’s oesophagus) secondary to gastro-oesophageal reflux disease (GORD) is recognised as the major cause of adenocarcinoma of the distal oesophagus. Studies have demonstrated that patients harbouring Barrett’s oesophagus carry a 30–125-fold increased risk for developing oesophageal adenocarcinoma as compared with...
the general population [10]. It is now understood that Barrett’s oesophagus and invasive carcinoma are linked through the intermediate step of epithelial dysplasia [5]. Dysplasia is termed low-grade or high-grade based on the degree of histological aberration, with more pronounced irregularities increasing the potential for carcinomatous change. While anti-reflux treatment may successfully convert low-grade dysplasia (LGD) back to non-dysplastic Barrett’s mucosa, the same is not true for HGD, which conveys cytological characteristics of malignancy and differs from invasive carcinoma only by lack of penetration through the basement membrane [11].

There remains some uncertainty regarding the natural history of Barrett’s oesophagus. In 2000 Reid et al. reported on 322 patients with Barrett’s oesophagus followed-up over a 15-year period. Surveillance endoscopy and biopsy identified HGD in 23% (75/322), of whom 59% (44/75) went on to develop adenocarcinoma within 5 years [12]. In contrast in 2001 Schnell et al. reported that only 16% of patients in their study group with HGD progressed to invasive cancer at a mean of 7.3 years [13]. Such disparity has further complicated our understanding of the natural history of HGD. The study by Schnell et al. has been criticised for having less rigorous biopsy protocols and relying on only one pathologist [14]. Nevertheless such reports continue to fuel the notion that HGD need not be managed with oesophagectomy, a procedure long perceived to be associated with unacceptably high morbidity and mortality, in the absence of evidence of invasive cancer.

Patients with HGD have a significant risk of harbouring occult cancerous foci. In 2000 Pellegrini and Pohl found that of 184 patients undergoing oesophagectomy for HGD, 43% (80/184) were found to have adenocarcinoma [15]. In the present study we found that 35% (8/23) of patients with a preoperative diagnosis of HGD alone had evidence of invasive cancer in resected specimens.

Recently, non-surgical treatment modalities such as EMR, endoscopic ablative therapies (including photodynamic therapy and argon plasma ablation) and rigorous endoscopic surveillance have attracted interest. Advocates of such techniques argue that in the absence of a preoperative diagnosis of invasive cancer, oesophagectomy is not necessary.

Endoscopic ablative techniques such as PDT and argon plasma coagulation use thermal or photochemical energy to ablate the abnormal epithelium and have been proposed as alternatives to surgery in the setting of HGD. A common complication of PDT is oesophageal structuring; the incidence of which ranges from 4.8% to 53% [16,17]. Other complications include bleeding, tracheo-oesophageal fistulae and occult oesophageal perforations [8]. Additionally a major disadvantage of these techniques is the inability to eradicate all the tissue with malignant potential, and following ablation foci of metaplastic epithelium are commonly left behind [18]. Squamous epithelium can cover these foci, masking them from future endoscopic visualisation [19], and moreover partially ablated metaplastic epithelium has been shown to develop aberrancy in its expression of proliferation markers and p53 [20].

Endomucosal resection offers the advantage of providing a pathological specimen to determine the extent and character of the lesion, and assess the adequacy of the resection. The risks of EMR include bleeding (1.2%), perforation (<5%) and stricture formation (9.4%) [21]. Moreover, studies have shown the technique to be associated with an up to 17% risk of recurrence of cancer at 12 months [7].

In light of the risks and questionable efficacies of invasive methods of treating HGD, some instead suggest a program of intensive endoscopic surveillance. This typically means endoscopy every 3–6 months with treatment withheld until biopsy-proven adenocarcinoma is discovered. Given the difficulties mentioned regarding definite diagnosis of HGD and differentiating it from invasive cancer this seems a perilous practice. In 2000 Weston et al. found that over a mean surveillance period of 36.8 months 4 out of 15 patients with HGD developed adenocarcinoma. They recommended that this method of expectant management be discouraged [22].

Older studies, not accurately reflecting current practices, are in part responsible for the perceived high morbidity and mortality associated with oesophageal resection. Many of these series were based on work at low volume, non-specialist centres, with operations performed on patients with advanced cancer. More recently improved preoperative staging allowing more careful patient selection, and intensive care advances have lead to a reduction in morbidity and mortality following oesophagectomy. Additionally centralisation of cancer service provision has had a significant impact. A recent paper by Kuo et al. looked at the impact of hospital volume on the clinical and economic outcomes following oesophageal resection. They found high volume practice to be associated with a 3.7 fold reduction in mortality [23].

With regard to our choice of operation, studies have demonstrated no significant difference in long-term survival or disease recurrence following either transthoracic or transhiatal oesophagectomy [24,25]. Moreover, the former may confer the advantage of reduced pulmonary morbidity. In the largest population based study to date comparing the two approaches, Chang et al. in 2008 concluded that transthoracic oesophagectomy confers an early survival advantage, with reduced 30-day mortality [25]. Though it has been posited that transthoracic dissection provides improved surgical exposure for harvesting of mediastinal lymph nodes, the long-term oncological benefits for this remain uncertain.
We report zero in-hospital mortality, acceptable morbidity, disease free survival of 96% (22/23) and an overall survival of 96% (22/23). This data provides additional evidence that transhiatal oesophagectomy for HGD can be performed with zero mortality and acceptable morbidity in a high volume centre, though we do acknowledge our small numbers.

5. Conclusion

We conclude that in experienced hands, at a high volume centre with appropriate patient selection and a dedicated upper GI histopathology unit, transhiatal oesophagectomy should remain the gold standard for patients with HGD. Of course we should continue to evaluate the less invasive therapies with the role of these being confined to those patients whose comorbidities preclude resection.

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