Available online at www.sciencedirect.com

ScienceDirect

EJSO 40 (2014) 77–84

EJSO the Journal of Cancer Surgery

www.ejso.com

Impact of specialized multi-disciplinary approach and an integrated pathway on outcomes in hilar cholangiocarcinoma

D. Gomez [a], P.B. Patel [a], C. Lacasia-Purroy [b], C. Byrne [a], R.P. Sturgess [d], D. Palmer [c], S. Fenwick [a], G.J. Poston [a], H.Z. Malik [a,*]

[a] North Western Hepatobiliary Unit, Aintree University Hospital NHS Foundation Trust, Longmoor Lane, Liverpool L3 4FG, UK
[b] Department of Anaesthesia, Aintree University Hospital NHS Foundation Trust, Liverpool, UK
[c] Department of Oncology, Aintree University Hospital NHS Foundation Trust, Liverpool, UK
[d] Department of Gastroenterology, Aintree University Hospital NHS Foundation Trust, Liverpool, UK

Accepted 13 October 2013
Available online 23 October 2013

Abstract

Aims: To assess the outcomes of patients with hilar cholangiocarcinoma following referral to a specialist multi-disciplinary team.
Methods: Over an 11-year period, patients referred with hilar cholangiocarcinoma were identified from a prospectively maintained registry. Collated data included demographics, operative findings and histo-pathological data. Survival differences and prognostic factors were determined.
Results: 345 patients were referred with hilar cholangiocarcinoma, of which 57 (16.5%) patients had surgery. Prior to 2008, of 143 patients referred, only 17 (11.9%) patients underwent surgery, compared to 40 (19.8%) of 202 patients referred from 2008 onwards ($p = 0.051$). In the surgery group, the majority of patients underwent left hemi-hepatectomy ($n = 19$). In addition, portal vein ($n = 5$), hepatic artery ($n = 2$) and inferior vena cava ($n = 3$) resections were performed. The R0 resection rate was 73.7%. The morbidity and mortality rates were 59.6% and 14.0%, respectively. The median disease-free survival was 16 (4–101) months. The presence of lymph node metastasis ($p = 0.002$) was the only predictor of poorer disease-free survival. The 5-year overall survival was 39.5% and was significantly better than that of the palliative group ($p < 0.001$).
Conclusions: Surgery is the optimal treatment option for patients with hilar cholangiocarcinoma and is associated with better overall survival. Prompt referral to tertiary centres with a core team of clinicians to manage this difficult condition may allow more patients to come to potentially curative surgical resections.

Keywords: Hepatectomy; Hepatic resection; Hilar; Cholangiocarcinoma

Introduction

Biliary malignancies constitute approximately 2% of all cancers found at autopsy, of which hilar or "Klatskin" tumours represent around 50–80% of these cases.[1–3] At present, it is unclear whether there is a true increase in the incidence of hilar cholangiocarcinoma (HC), or additional cases are being identified with more accurate cross-sectional imaging being performed.

The overall 5-year survival rates following hepatic resection of HC varies from 20 to 40%.[4–7] Although surgery remains the only potential curative therapy, it is technically demanding due to the presence of locally advanced disease, proximity of the tumour to hilar vasculature and tumour biology. Various clinico-pathological variables have been shown to influence survival, including margin status, nodal status, tumour differentiation and peri-neural and/or vascular invasion.[4,7–9] However, the majority of patients with HC are unresectable at either presentation, following staging laparoscopy or during laparotomy. Criteria for unresectable disease include locally advanced tumours involving portal and hepatic vasculature, distant metastases and nodal metastases beyond the hepato-

* Corresponding author. Tel.: +44 151 529 2740; fax: +44 151 529 8547.
E-mail address: Hassan.Malik@aintree.nhs.uk (H.Z. Malik).

0748-7983/$ - see front matter © 2013 Published by Elsevier Ltd.
http://dx.doi.org/10.1016/j.ejso.2013.10.009

duodenal ligament. In addition, patients must have limited co-morbidities; as most cases require an extended hepatectomy against a background of cholangitis and obstructive jaundice.

The improved treatment of HC over the last decade is not only related to changes in surgical strategy, but also improvement in selection and pre-operative work-up of patients considered for curative resection. With the introduction of specialist multi-disciplinary team (MDT) management, this treatment process may contribute to better outcomes.[10] The aim of this study was to assess the outcomes of patients with HC following such a specialist MDT approach.

Patients and methods

Patients with HC referred during an 11-year period from January 2001 to December 2012 were identified from a prospectively maintained hepatobiliary database and specialist multi-disciplinary recording system.

Patients that had potentially resectable and unresectable HC were included. In addition, intra-hepatic cholangiocarcinoma affecting the portal hilum (often termed peri-hilar cholangiocarcinoma) were included, as the treatment is similar and often difficult to differentiate from true HC. Patients with gallbladder cancer, peripheral intra-hepatic and distal cholangiocarcinoma were excluded.

Pre-operative evaluation

Collated data included patient demographics, surgery, histopathology analysis and outcome. Pre-operative assessment included multi-slice triple phase contrast-enhanced computer tomography (CT) scan of the thorax, abdomen and pelvis, and liver-specific contrast enhanced magnetic resonance imaging (MRI) of the liver (from 2008).

Pre-operative biliary drainage was considered in patients with obstructive jaundice. Biliary drainage of the future liver remnant was achieved endoscopically, percutaneous drainage avoided whenever possible. Endoscopic retrograde cholangio-pancreaticography (ERCP) is used to specify the anatomic location of the tumour, grade it according to the Bismuth classification and obtain tissue diagnosis.[11] In our unit, single-operator cholangioscopy (RPS) is used in selected cases to obtain detailed information of the distal extent of the lesion and to obtain targeted biopsies. Diagnosis could be confirmed by brush cytology; however, this finding was not a pre-requisite for undergoing resection. In jaundiced and malnourished patients, where the future liver remnant was obstructed, a removable metal stent was placed across the lesion for biliary decompression.[12] Since 2008, all jaundiced patients with suspected HC had their biliary stenting performed in our unit. If cross-sectional imaging suggests the lesion is resectable, the patient then undergoes a formal anaesthetic assessment.

Staging laparoscopy was performed routinely in all patients deemed resectable on pre-operative cross-sectional imaging and considered fit for surgery. This investigation was performed to exclude the presence of peritoneal carcinomatosis, extra-hepatic metastases, and locally advanced hilar disease. If there is no contra-indication to resection following laparoscopy, the patient was scheduled for laparotomy with a view to resection.

Multi-disciplinary approach

All patients were discussed in a specialist MDT meeting that consisted of hepatobiliary surgeons, hepatologist, oncologist, radiologist and pathologist prior to surgery. Since 2008, an integrated care pathway was implemented, and jaundiced patients with a proximal biliary stricture were managed by a specialist MDT.

Surgical and post-operative details

Parenchymal transection was performed using the Cavi-Pulse Ultrasonic Surgical Aspirator (CUSA) or Kellyclasia. Intra-operative ultrasound was performed to confirm the findings of pre-operative imaging. The number of hepatic (Couinaud's) segments[13] resected was determined by the procedure performed as stated in the Brisbane nomenclature.[14] The type of surgical procedure was dependent on the resection of all macroscopic disease and achieving a clear resection margin, while preserving sufficient remnant liver. Resection of the caudate lobe was always performed. Intermittent Pringle manoeuvre was used during liver transection if required. Lymphadenectomy was performed routinely and consisted of removal of all lymph nodes and connective tissue in the hepato-duodenal ligament and the retro-duodenal area. Both distal and proximal margins of the sectioned bile ducts were sent intra-operatively for frozen section examination. The presence of neoplastic cells in these examined sections constituted an indication to extend the resection margins within the hepatic parenchyma as appropriate, within the feasibility to construct multiple segmental biliary-enteric anastomoses. Roux-en-Y biliary enteric reconstruction was performed using a 70 cm segment of proximal jejunum. Vascular reconstructions of portal vein or hepatic artery were performed when required and technically feasible to achieve R0 resections in patients with pre-operatively unrecognized vessel involvement on cross-sectional imaging. Since 2008, all HC cases were performed by two surgeons (HZM, SF).

Since 2008, all patients listed for surgery underwent cardiopulmonary exercise testing (CPET) and were assessed pre-operatively by an anaesthetist (CLP) who is a core member of the MDT. Furthermore, all cases were performed by only two anaesthetists.

Post-operative morbidity and 30-day mortality were recorded. Mortality was defined as any death during post-operative hospitalization or within 30 days following