Surgical possibilities for bile duct cancer: Standard surgical treatment

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Summary

There is no consensus on the surgical treatment of bile duct cancer, which varies from total nihilism to an extremely aggressive resectional policy. This paper describes the adoption of a ‘middle road’ approach to these difficult cancers, and suggests that selective use of stenting, bypass and resection with judicious application of adjunctive chemotherapy is an appropriate attitude until controlled studies of the alternatives are available. The main aims of treatment are (a) relief of obstructive jaundice, (b) prevention and treatment of future recurrent obstruction and cholangitis, and (c) eradication of tumour when possible. Local resection carries a low morbidity and mortality and is always a reasonable option in patients fit for surgery, but the relative value of non-radical resection and stenting with chemotherapy remains to be determined. Extended resections, including major hepatectomy and radical lymph node dissection, are only justified when the intent is curative, and some patients may not be suitable for such extensive surgery. In patients who are explored and determined to be unsuitable for major resection, surgical bypass is an option, but there is little evidence that this produces better palliation or quality of survival than optimal percutaneous or endoscopic stenting.

Of 76 patients referred to the author over 7 years, 27 (35%) underwent surgical resection, and 23 (30%) had no operation. In patients followed up for more than 1 year, median survival following curative resection (9 patients) was 26 months, and after palliative resection (15 patients) it was 11 months. Median survivals after palliative biliary-enteric bypass (11), exploration alone (9), or no operation (20) were 2, 4, and 5 months respectively. A cautious and selective approach to surgery for these tumours is advocated.

Key words: bile duct cancer, biliary bypass, biliary resection, liver resection, palliation, stenting

Introduction

Bile duct cancer remains one of the most challenging tumours for the surgeon and for the medical oncologist. Pre-operative diagnosis is difficult, no staging system has been universally adopted, and there is no consensus regarding the indications for or the extent of surgical management of these patients. Therefore to speak of ‘standard’ or ‘conventional’ surgery for such tumours is to make unjustifiable assumptions about current surgical practice. Moreover, practice has changed over recent years from a completely nihilistic approach to hilar tumours to recognition of the role of resection, as well as the re-evaluation of other modalities of treatment. At the same time, major technical advances in endoscopic and percutaneous stenting technology has led to a wider adoption of these methods of treatment, which in many cases appear to rival the efficacy of operative management. For the purpose of this review, I will regard ‘conventional’ surgery as encompassing all operations except those which include extended resection and reconstruction of major vessels or radical lymphatic dissection, both of which are dealt with in a subsequent article. ‘Conventional’ surgery in this context therefore consists of resections of the biliary tree, with or without liver resection, and biliary-enteric bypass procedures. I will not discuss surgical intubation procedures, which have been largely superseded by non-operative intubation methods.

Assessment of the patient

This is aimed both at pre-operative staging of the tumour to determine resectability and to plan alternative approaches for tumours deemed irresectable, and at assessment of the general fitness of the patient for invasive treatment methods. The assessment of the tumour staging is largely based on radiological investigations.

Radiology

Initial assessment is almost invariably by ultrasound (US), but since this is generally performed to elucidate the cause of jaundice the initial US examination rarely gives accurate staging information. The level of obstruction and to some extent its laterality can be defined readily, but its nature may remain unclear. The older literature stated that a mass was rarely seen on US in cholangiocarcinoma, but this has been superseded by improvements in radiological technology, and either a mass or periductal thickening can be identified in most cases [1]. More detailed US examination will also allow definition of the level of obstruction to individual segments, demonstrate segmental hepatic duct dilatation, and evaluation of vascular invasion or encasement, especially that of the portal vein and its segmental branches. In many cases of hilar tumours, US with colour Doppler flowmetry may be sufficiently detailed to obviate the need for any further angiographic techniques [2].

Cholangiography is the mainstay of pre-operative assessment of the extent of invasion of the biliary tree, on which the decisions for conventional treatment rely. In the UK and most of continental Europe ERCP has become so widely available that it is now uncommon to receive patient referrals to specialist centres for treatment of cholangiocarcinoma without prior ERCP and often endoscopic stenting. This is not always an advantage, as stents are usually placed with a view to prompt relief of...
obstructive jaundice, and the level of detailed cholangiography obtained may be insufficient for pre-operative staging. In addition, it is not always possible to direct an endoscopic stent to the most appropriate segmental duct for drainage, and selective cannulation of an obstructed and atrophic segment may be at best ineffective and at worst counter-productive, by introducing infection into a previously sterile segment of liver [3]. Moreover, a stent may effectively obscure the visualisation of the hilar ducts for staging purposes. It is often necessary to remove such a stent and repeat the cholangiography either by repeat ERC or by percutaneous transhepatic cholangiography (PTC). It is the author's preference to delineate all hepatic segmental ducts by PTC in cases judged to be potentially resectable, and if this has not been achieved by ERC, then early PTC is performed.

The question of pre-operative drainage remains controversial. Some authors perform routine percutaneous drainage (PTBD), and attempt to traverse the obstructing tumour to achieve internal bile flow in all cases: the catheter can be found in the duct below the tumour during the resection, making identification easier [4]. The Nagoya group (reported in the next paper) perform multiple segmental PTBD, and use this not only for biliary decompression and relief of jaundice, but also for percutaneous cholangioscopy and biopsy for precise ductal staging of the tumour [5]. It is the author's practice to perform PTBD only in cases of severe ongoing sepsis, particularly if complicated by renal failure, or when major liver resection is planned in a deeply jaundiced patient.

Angiography can be used very selectively, in patients in whom US has suggested vascular involvement, but has failed to define its extent precisely. CT and MRI scanning are invaluable for staging cholangiocarcinoma, and may show a tumour mass or periductal invasion, vascular perfusion defects, and delineate segmental biliary occlusion or atrophy with excellent clarity. Moreover, these axial imaging methods may be the best means of demonstrating lymph node enlargement suggestive of tumour metastasis. So far, CT, MR and US are complementary investigations, each with strengths and weaknesses, and are often best used in combination. MR cholangiography may in the future replace invasive biliary imaging, but at present the definition is insufficient for detailed planning of surgical resections.

Overall radiological staging

Synthesis of the findings of these investigations should allow identification of patients resectable by 'conventional' surgery. It is easiest to define those criteria which exclude patients from this category:

(a) hepatic duct involvement beyond the main sectoral duct confluence on both sides of the liver
(b) major involvement of the main stem of the portal vein
(c) bilateral portal venous involvement
(d) lymph node enlargement beyond the immediate region of the bile duct and proper hepatic artery
(e) metastases to other sites.

The main point of discussion lies in (a) and (b). Involvement of the confluence of the anterior (5 & 8) and posterior (6 & 7) sectoral ducts on the right side can be managed by right or extended right hepatectomy, provided there is no involvement beyond the umbilical fissure on the left side. Any greater extent than this would require complex surgical resection and reconstruction, and while this is technically possible, it goes beyond the scope of what we should regard for the purpose of this paper as 'conventional' surgery. The issue of major portal venous resection and reconstruction has been widely debated. Results to be presented in the next paper demonstrate that survival is much worse in patients who undergo such resections than in cases where these are not required, but whether such procedures are worthwhile will continue to be matter of fine judgement. It is the author's view that this may be justified in selected cases, particularly for patients who are young and fit and who have otherwise well-localised disease.

Clinical assessment

Judgement of resectability requires also a general assessment of the patient's physical condition, and co-morbidity (e.g., diminished respiratory or cardiac reserve) will alter the operative strategy. Major liver resection is usually contraindicated in cases where hepatic function is impaired by underlying cirrhosis, active hepatitis, or significantly fatty liver, though this combination may be very unusual in cases of biliary tract cancer. Most centres use some variant of the Child-Pugh grading to assess liver function, and this gives a crude but usually adequate measure of likely functional reserve. Other groups have used a more sophisticated approach, assessing functional reserve by dynamic tests, such as ICG clearance [6]. This has been extended to the use of pre-resection selective portal vein embolisation to promote contralateral hyperplasia and allow safer or more extensive resections [7]. Pre-operative biliary decompression will often promote improvement in liver function which will permit safer resection, and it has already been noted that some authors use this technique routinely and others selectively. The presence of marked atrophy in a chronically-obstructed segment makes that part of the liver unsuitable as a liver remnant, so this is a relative contraindication for liver resection.

Operative strategy

Initial Assessment

Laparoscopic staging has found a valuable place for pancreatic tumours [8], but has not been widely reported for cholangiocarcinoma. It may obviate unnecessary laparotomy in cases of diffuse intra-peritoneal spread, but this is not a common occurrence in the case of otherwise resectable tumours.

A limited laparotomy is sufficient to assess any intraperitoneal metastases, and doubtful lesions can be removed and submitted to frozen section examination. A combination of palpation and intra-operative ultrasound may be used to detect unsuspected liver metastases, which may preclude resection depending on their distribution. If the tumour appears to be resectable (according to the criteria of the surgeon), then the abdomen may be opened more widely and trial dissection commenced.
Local resection

Using criteria for 'conventional' surgery, major involvement of the portal vein or deep invasion of the caudate lobe at the hilus may contraindicate resection. It may therefore be useful to avoid division of the distal bile duct until it has been established that adequate hepatic ducts will be available for anastomosis after local resection. Early lowering of the hilar plate above the confluence of the hepatic ducts will reveal tumour invasion beyond the chosen acceptable limits for resection, and particularly if there has been adequate palliation by means of previous endoscopic or transhepatic drainage the procedure may be abandoned at this stage, following adequate tumour biopsy for histological grading and to allow consideration of palliative chemotherapy. If the proximal part of the tumour can be cleared, then division of the distal bile duct behind the pancreas will allow progressive mobilisation of the extrahepatic biliary tree from the portal vein and hepatic arteries, usually along with associated peri-arterial lymphatics en bloc. If invasion of the portal vein is discovered at a late stage during this mobilisation, a decision must be made about resection and reconstruction. Partial or even circumferential resection of the wall of the vein which has limited tumour invasion is within the limits of 'conventional' surgery: major resection with vein grafting is in the category of 'extended' resection and is described elsewhere in this section.

Liver resection

For tumours extending into the right or left liver, extension to include resection of the involved lobe is performed. The evidence that the caudate lobe is very frequently involved by hilar tumours is very convincing, and this lobe should usually be included in the resection.

Biliary reconstruction

Hepaticojejunostomy is performed to all transected ducts. This may involve from one to five or more duct orifices: the number can be reduced by judicious apposition and suturing of adjacent segmental ducts, but care must be taken not to produce tension when doing this. Practice differs regarding the use of intra-operative frozen section to confirm tumour clearance: many pathologists find great difficulty in distinguishing well-differentiated cholangiocarcinoma from inflammatory changes due to biliary obstruction on frozen section, especially after prolonged intubation. If possible, tumour clearance should be confirmed histologically, but sometimes it is necessary to rely on macroscopic appearances.

It is the author’s practice to use a 70cm Roux-en-Y loop for the jejunal limb, and to construct the anastomosis in a single layer of interrupted, mucosa inverting, absorbable sutures: 4.0 or 5.0 PDS is an ideal material for this. We also routinely construct a jejunal 'access loop' at the blind end of the jejunum, fixed to the peritoneum of the abdominal wall in a convenient position to provide a short, straight, laterally-placed track from the end of the loop to the reconstructed hilus. The blind end is marked at the point of fixation to the peritoneum of the abdominal wall with a metallic marker: a circular suture of 2.0 stainless steel is easy to apply and is readily visible on plain abdominal radiography for future percutaneous puncture, intubation, and biliary imaging or intervention if this should become necessary during follow-up. The procedure adds little time to the operation, carries no significant morbidity, and provides 'insurance' against future biliary stenosis due to fibrous stricture formation or local tumour recurrence.

The use of trans-anastomotic tubes reflects individual practice. There is no good evidence that prolonged use of such tubes prevents stricture formation or promotes healing, and some reasonable grounds to believe they may actually be deleterious. It is useful however to leave a fine tube across the anastomosis in order to obtain a post-operative check cholangiogram, which will serve as the basis for future comparison in the event of recurrence of biliary obstruction. It is the author’s practice to place such tubes routinely, and to remove them after a cholangiogram at 7 days.

Bypass

For irresectable tumours, if adequate palliation has not already been secured by pre-operative intubation and internal biliary drainage, the option of biliary-enteric bypass should be considered. Permanent external biliary drainage is not regarded as satisfactory long-term palliation. In such cases, an approach to the duct of segment 3 can be made to the left of the falciform ligament, or in the umbilical fissure. The technique has been well-described, and there is some evidence (though not in controlled studies) that this may provide better long-term palliation and freedom from recurrent cholangitis than permanent plastic stents [9]: similar evidence has not been produced comparing surgical bypass with metallic stents. Similar approaches to the right-sided segmental ducts are possible, though technically more difficult. It is important to avoid use of chronically obstructed and atrophic hepatic segments for such bypass, as this may be ineffective and possibly cause harm by introducing infection into a previously sterile closed segment. It has been well demonstrated that drainage of one liver lobe with good function is adequate for palliation in most cases, and drainage of all hepatic segments, though ideal, is not essential [10].

Adjunctive treatment

Cholangiocarcinoma has been traditionally regarded as a chemo-resistant tumour. However, experience with combination chemotherapy such as ECF (epirubicin, cisplatin, and 5-fluorouracil) for other sites in the GI tract has led to the use of similar regimens for cholangiocarcinoma with some good results [11]. However, controlled clinical trials are needed both for palliatively treated tumours, and for adjuvant therapy after apparent radical tumour resection. Downstaging of cholangiocarcinoma by means of 'neo-adjuvant' chemotherapy, as in some other GI tumours, is an attractive but unproven concept.

Management of recurrence

In the past, recurrence of jaundice after treatment of cholangiocarcinoma was presumed to indicate advanced
disease and patients were treated very conservatively, often with referrals for terminal care. It must be recognised that many patients can receive effective further palliation by use of interventional radiological or endoscopic procedures, and all but those who clearly have advanced generalised disease should be offered further evaluation and intervention as appropriate. Some cases of recurrent jaundice may be due to benign stricture formation, especially if there have been multiple difficult hilar anastomoses, and these may be effectively treated by balloon dilatation. Those who truly have local recurrence can be stented, and self-expanding metallic stents are particularly useful in these cases.

Conservative surgery: results

Data from the author's previous experience in Hammersmith Hospital, London [12], using similar criteria for resection showed that mortality was directly related to major liver resection in the presence of previous surgery or infected biliary drainage. The survival after liver resection (16 patients) did not differ from that for local resection (11 patients), and there was no mortality in the latter group. Survivors of the resections lived for a median time of 25 months, and the main determinant of long-term survival was histological clearance at the resection margins. In subsequent experience at King's College Hospital, the author received referrals for treatment of cholangiocarcinoma in 76 patients over 7 years. The age ranged from 22 to 75 years (mean 59 years). The majority (85%) of tumours were at the hilus (Bismuth type II - 51, and types IIIa or IIIb - 11). Using criteria along the lines described above, 23 patients had no operative treatment. Of the 53 who underwent operation with a view to resection, 14 (26%) had no definitive procedure, most having been effectively stented prior to operation. Twelve (23%) had only a bypass procedure. Overall, 32 (60%) patients had advanced intra-abdominal disease at the time of operation (11 lymph node metastases, 7 peritoneal spread, and 11 both, with 1 case each of pancreas, gallbladder, IVC and main portal vein invasion). Twenty-seven patients (35% of all referrals and 51% of those explored) underwent surgical resection (19 local extrahepatic biliary resection, 4 pancreatoduodenectomy, 2 left hepatectomy, 1 right hepatectomy, and 1 extended left hepatectomy). There were no peri-operative (30-day or inhospital) deaths. All the hepatic resections were performed with curative intent, but 18/19 local resections were regarded as palliative (involved resection margins or residual tumour in lymph nodes or on the portal vein). The crude survival data for these groups is shown in Table 1: 12 patients operated on during the last year have been excluded from the analysis because of short follow-up.

Conclusion

'Conventional' surgery, with a highly selective approach to major liver resection and vascular reconstruction, and a more inclusive approach to local, palliative, resection, may still confer survival advantage, with low peri-operative morbidity and mortality. Stenting remains a useful fall-back for irresectable patients, and the true value of adjunctive chemotherapy remains to be finally evaluated in controlled studies. Studies comparing more extensive surgical approaches with 'conventional' surgery may be difficult to achieve, but careful comparison of staging data and survival results should be made. Objective and prospective assessment of quality of life, taking account of the morbidity of major surgery, has never been fully addressed in patients with this difficult tumour.

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<th>Lost to follow-up</th>
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<td>4</td>
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<td>9</td>
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<td>Curative resection</td>
<td>9</td>
<td>-</td>
<td>3*</td>
<td>6</td>
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* 1 with no evidence of disease
* 2 with no evidence of disease

References


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