A Single-Center Experience in the Management of Altemeier-Klatskin Tumors

Konstantinos Tsalis¹, Konstantinos Vasiliadis¹, Vasilios Kalpakidis², Emmanuel Christoforidis¹, Antonios Avgirinos¹, Dimitrios Botsios¹, Angelos Megalopoulos¹, Anna Bettina Haidich⁴, Dimitrios Betis¹

¹) Fourth Surgical Department, Aristotle University. 2) Department of Radiology and 3) Department of Gastroenterology, General Regional Hospital “George Papanikolaou”. ⁴) Laboratory of Hygiene, Medical School, Aristotle University, Thessaloniki, Greece

Abstract

The aim of this study is to present our experience in the management of patients with Altemeier-Klatskin tumor, with particular focus on the risk factors that influence survival after tumor resection. Methods. Over a 15-year period, 37 patients with hilar cholangiocarcinoma were managed in our Department. The mean age of the patients was 62.5 years. Twenty-one patients were treated by palliative measures while sixteen patients had resection of the tumor and 11 of these had negative histological margins. An associated major hepatectomy was performed in six. In parallel, certain risk factors that could influence survival were analyzed. Results. The resectability rate was 43.2%. The 30-day mortality rate was 7.4% and postoperative morbidity was 37.5%. The sites of the resected tumors were Bismuth-Corlette type I lesions in 3 patients, type II in 6, type IIIa in 2, and type IIIb in 5. The median survival of patients undergoing resection was significantly higher than of patients not undergoing resection (p<0.001). Furthermore, patients with R₀ resection and histological clear margins experienced significantly superior survival than patients with R₁ resection and positive margins (p=0.001, and p<0.001 respectively). Resections resulting in cancer-positive margins did not portend a survival benefit. Conclusion. Negative surgical margins, tumor differentiation and infiltrating macroscopic appearance, were statistically significant prognostic factors. Our findings emphasize that complete resection of the tumor with negative histological margins offers the best possibility of long-term survival, and that the addition of hepatectomy to biliary resection results in a greater number of patients with margin negative resections.

Key words
Hilar cholangiocarcinoma - Klatskin tumor - hepatectomy - intrahepatic anastomosis

Introduction

Altemeier-Klatskin tumor is a rare malignant neoplasm, arising from the bile duct epithelium of the common hepatic duct or its first and second bifurcation (1,2). This tumor was previously considered to be only rarely liable to radical resection, and palliative treatment in terms of operative biliary drainage was the accepted therapeutic approach (3,4). To date, the spectrum of the therapeutic modalities varies and includes the curative approach by performing radical excision of the lesion and the palliative approach in which a surgical bypass or even percutaneus or endoscopic stent insertion can be performed, with or without adjuvant therapy (5,6).

More recently the majority of hepatobiliary surgeons appear to agree with the concept of concomitant hepatectomy when performing resectional surgery for hilar bile duct cancer in terms of both obtaining a negative resection margin and increasing the number of resectable patients, offering the possibility of long-term survival (7-11).

The aim of our study is to present our experience in the management of patients with Altemeier-Klatskin tumor, with particular focus on various risk factors that influenced survival after tumor resection.

Patients and methods

Between 1991 and 2006, a total of 37 consecutive patients with hilar cholangiocarcinoma were managed in our Department. There were 10 women and 27 men with a median age of 63 years (range 37-87 years). All patients were jaundiced. Nineteen patients had epigastric or right subcostal pain, 17 patients had severe weight loss and 4 had fever. Six patients had prior inappropriate surgery. In particular, 4 had cholecystectomy and 2 patients had exploratory laparotomy without a definitive procedure prior to the diagnosis of Altemeier-Klatskin tumor, and were referred to our Department from other hospitals 10 to 170 days after their initial operation.

Preoperative biliary drainage was used in 15 patients in order to decrease the operative risk of a major surgical
Tumors were considered unresectable. Preoperative biliary drainage was performed when serum bilirubin levels were more than 10mg/dL (12,13). Our policy was to drain only the remnant liver based on planned hepatectomy. Percutaneous transhepatic drainage of the remaining liver lobe was performed in 14 patients and endoscopic insertion of two Amsterdam type stents in one.

Laboratory tests showed cholestatic jaundice with a mean bilirubin of 21.7 mg/dL (range 5-41 mg/dL). Preoperative workup also included doppler ultrasound in 33 patients (89.2%), computed tomography (CT) in 34 (91.9%), endoscopic retrograde cholangiopancreatography (ERCP) in 7 patients (18.9%), percutaneous transhepatic cholangiography (PTC) in 24 (64.9%), magnetic resonance imaging - magnetic resonance cholangio-pancreatography (MRI-MRCP) in 16 (43.2%) and cholangiography via the T-tube in 4 (10.8%). Special attention was given to liver function tests, coagulation results and albumin levels.

Tumors were divided preoperatively into four anatomic types according to the modified Bismuth-Corlette classification system (14). The classification was based on preoperative and intraoperative cholangiographic data and in cases of surgical intervention on the macroscopic pathological appearance of the lesion. Postoperative staging was performed according to the American Joint Committee on Cancer 2002 guidelines (15).

The criteria used to establish unresectability of the tumor were based on patients’ characteristics (inability to tolerate a major operative procedure, cirrhosis), local factors (hepatic duct involvement up to secondary radicles bilaterally, encasement of main portal vein, encasement of both branches of the portal vein, encasement of the portal vein of one lobe of the liver combined with encasement of the hepatic artery of the other lobe, combination of vascular encasement to the one side of the liver with extensive bile duct involvement of the contralateral site, atrophy of one liver lobe with encasement of contralateral portal vein branch and atrophy of one liver lobe with contralateral secondary biliary radicle involvement) and the presence of distant disease (histologically proven nodal disease in N2 lymph nodes, and lung, remaining liver, or peritoneal metastases) (16,17). Hepatic lobar atrophy was considered present if CT or MRI demonstrated a small, often hypoperfused lobe with crowding of dilated intrahepatic ducts (18). Portal vein involvement was defined radiographically as compression or narrowing, encasement, or occlusion.

All patients who did not fulfill the unresectability criteria were considered as candidates to undergo a potentially curative surgical procedure. In our Department the standard surgical intervention for Bismuth-Corlette type I and II was resection of the common bile duct with the bile duct confluence, the gallbladder and the lymphatic and connective tissue of the hepato-duodenal ligament. The resection included the caudate lobe in cases of posterior infiltration by the tumor into the liver parenchyma. For type III tumors hilar resection was carried out in combination with hemihepatectomy and caudate lobe resection. Type IV tumors were considered unresectable.

Proximal and distal bile duct surgical margins were routinely submitted for frozen section examination. If the margins were positive for cancer cells, an additional resection, whenever technically feasible, was carried out to achieve a clear margin. We defined potentially curative resection as an operation with histologically clear margins of the bile ducts at both ends, along with extirpation of metastatic regional lymph nodes, in the absence of metastases. Patients who underwent a potentially curative procedure were then further stratified into those with negative (R0) and positive (R1) histological margins while as R2 were classified patients with macroscopic residual tumor.

Intraoperative US and the application of the posterior approach to the hepatic hilus were used for the intraoperative assessment of resectability (19,20). Exposure of the hepatic confluence for vascular assessment was accomplished by transaction of the common bile duct above the duodenum, with reflection superiorly. Hepatic resection and/or caudate lobe excision was performed to achieve histologically negative margins. The evaluation of the extent of the disease was based on the intraoperative and pathological findings. Operative mortality was defined as death during hospitalization or within 1 month after surgery. According to our treatment protocol, all patients after tumor resection were planned to receive chemoradiation therapy. Follow-up ranged from 5 to 114 months.

**Statistical analysis**

The survival curves among groups were compared with the Log-rank test and were presented graphically with the Kaplan-Meier plots. Analyses were conducted in SPSS 13.0 (SPSS, Inc., Chicago, IL). All reported p-values are two-tailed with p <0.05 considered as significant.

**Results**

Tumor resection was achieved in 16 patients (resectability rate 43.2%). Among these, 11 (68.7%) patients had a potentially curative procedure (R0), while four (25%) had R1 and one (6.2%) R2 resection. Eleven patients had a hilar resection only. In these, a Roux-en-Y cholangiojejunostomy to the primary or secondary hepatic ducts established biliary continuity. Five patients had a combined tumor and liver resection. In particular, these patients underwent tumor resection and left (4) or right (1) hepatectomy in combination with caudate lobe (segment I) resection, as long as we accept that resection of segment I should be routinely performed when hepatic resection is required.

The resected tumors were Bismuth-Corlette type I lesions in three patients (18.7%), type II lesions in 6 (37.5%), type IIIa lesion in 2 patients (12.5%) and type IIIb lesions in 5 patients (31.25%). Macroscopically, the tumor was of nodular type in 6 patients, papillary type in 2 and infiltrating in 8 patients. According to the TNM classification 3 tumors were spreading to the muscular layer (T3), 6 to the perimucosal connective tissue (T4) and 7 were displaying periductal...
Three patients had a stage I disease, 6 patients a stage II disease and 7 patients a stage IVa disease. Negative lymph node status (N0) was found in 14 and metastatic lymph nodes (N1) were found in 2 patients. The differentiation of the tumor was well in 5 patients, moderate in 5 and poor in 6 patients.

Eleven patients fulfilled preoperatively the unresectability criteria. Two of these patients were classified as ASA IV, 3 patients proved to have metastatic disease, 4 patients had type IV lesions and 2 had portal vein occlusion according to the data of preoperative workup. In 6 of the patients who had high bilirubin levels (>10mg/dl), a percutaneous transhepatic biliary drainage was performed and finally a metal stent was placed in 4 of them, in order to offer jaundice relief.

In 10 patients the tumor proved to be unresectable according to the intraoperative findings. Four of these patients had peritoneal carcinomatosis and 6 evidenced encasement of the main portal vein in the tumor, proximal to its bifurcation. To these patients, surgical palliation was offered. In particular, right intrahepatic Roux-en-Y hepaticojejunostomy was performed in 3 patients, in 6 patients a transtumoral intubation was employed and one patient underwent a Roux-en-Y double biliointestinal bypass procedure (right hepatic and duct of segment III Roux-en-Y biliojejunostomy).

Of the 16 patients who had tumor resection, one died on the 12th postoperative day from myocardial infarction, giving an operative mortality of 7.4%. There were no operative deaths after hepatectomy. Overall postoperative morbidity occurred in 6 (37.5%) patients. Postoperative complications were biliary fistula in one patient, which resolved spontaneously on the 20th postoperative day, pleural effusion/atelectasis in two, peroneal nerve paresis in one, ascites in one, and wound infection in one. Among the 10 patients managed by surgical palliation, one died on postoperative day 5 due to septic shock. Septic complications developed also in another 2 patients, each of whom was successfully conservatively managed.

The Kaplan-Meier survival of the overall group of 16 patients at 1, 3 and 5 years was 86%, 64% and 21%, respectively. The median survival of patients undergoing resection was significantly higher than of patients who did not undergo resection (median: 38 vs. 9 months, p<0.001, Fig.1). Although older patients seemed to have better survival than younger, there was no significant difference in survival according to age (p=0.732, Table I).

The resection was judged to be curative (R0) in 11 (69%) patients, and the median survival of these patients was 23 months. In one patient, the resection was macroscopically palliative (R2) and could not be extended further. He was stage IVa and survived 12 months. Four patients had microscopically palliative resections (R1) as determined by subsequent pathological evaluation: two stage II (local excision), and two stage IVa (the first underwent tumor resection, and left hepatectomy with caudate lobectomy while the second underwent local excision because the procedure could not be extended further). Patients with R2 resection experienced significantly longer survival than patients with R0 resection (median: 39 vs. 20 months, p=0.001, Fig.2). The median survival of patients with R1-R2 resections was 12 months, while for patients not undergoing resection it was 9 months: this difference however was not statistically significant (p=0.483). Also, patients with histologically clear margins had significantly greater survival than patients without clear margins (median: 39 vs. 12 months, p<0.001, Fig.3). There was no significant difference in survival according to the type of surgery (local excision vs. local excision plus hepatectomy, Table I). Similarly, there was no significant difference in survival according to Bismuth-Corlette type lesions, to TNM staging or TNM classification and lymph node involvement (Table I).
Table I 1-year, 3-year and 5-year survival after resection according to different prognostic factors

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>1-year (%)</th>
<th>3-year (%)</th>
<th>5 year (%)</th>
<th>(Min-Max)</th>
<th>p-value a</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;60 years</td>
<td>6</td>
<td>80</td>
<td>40</td>
<td>-</td>
<td>(11 – 30)</td>
<td>0.732</td>
</tr>
<tr>
<td>60-70 years</td>
<td>7</td>
<td>85.71</td>
<td>68.57</td>
<td>22.86</td>
<td>(6 – 114)</td>
<td></td>
</tr>
<tr>
<td>≥ 70 years b</td>
<td>3</td>
<td>100</td>
<td>-</td>
<td>-</td>
<td>(5 – 20)</td>
<td></td>
</tr>
<tr>
<td><strong>Bismuth-Corlette type</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.533</td>
</tr>
<tr>
<td>I b</td>
<td>3</td>
<td>100</td>
<td>-</td>
<td>-</td>
<td>(18 – 20)</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>6</td>
<td>83.33</td>
<td>66.67</td>
<td>33.33</td>
<td>(6 – 114)</td>
<td></td>
</tr>
<tr>
<td>IIIa+IIIb</td>
<td>7</td>
<td>80</td>
<td>53</td>
<td>0</td>
<td>(5 – 38)</td>
<td></td>
</tr>
<tr>
<td><strong>TNM staging and classification</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.512</td>
</tr>
<tr>
<td>Ib (T1)</td>
<td>3</td>
<td>100</td>
<td>-</td>
<td>-</td>
<td>(18 – 31)</td>
<td></td>
</tr>
<tr>
<td>II (T2)</td>
<td>6</td>
<td>83.33</td>
<td>66.67</td>
<td>33.33</td>
<td>(6 – 114)</td>
<td></td>
</tr>
<tr>
<td>IVa (T3)</td>
<td>7</td>
<td>80</td>
<td>53</td>
<td>0</td>
<td>(5 – 38)</td>
<td></td>
</tr>
<tr>
<td><strong>Lymph nodes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.824</td>
</tr>
<tr>
<td>Negative</td>
<td>14</td>
<td>84.60</td>
<td>59.20</td>
<td>29.60</td>
<td>(5 – 114)</td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>2</td>
<td>100</td>
<td>100</td>
<td>0</td>
<td>(11 – 38)</td>
<td></td>
</tr>
<tr>
<td><strong>Macroscopic appearance</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.049</td>
</tr>
<tr>
<td>Nodular+papillary</td>
<td>8</td>
<td>100</td>
<td>100</td>
<td>50</td>
<td>(14 – 114)</td>
<td></td>
</tr>
<tr>
<td>Infiltrating</td>
<td>8</td>
<td>68.57</td>
<td>34.29</td>
<td>0</td>
<td>(5 – 39)</td>
<td></td>
</tr>
<tr>
<td><strong>Histology</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.046</td>
</tr>
<tr>
<td>Well b</td>
<td>5</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>(19 – 114)</td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>5</td>
<td>100</td>
<td>100</td>
<td>0</td>
<td>(5 – 38)</td>
<td></td>
</tr>
<tr>
<td>Poor</td>
<td>6</td>
<td>62.50</td>
<td>29.83</td>
<td>0</td>
<td>(6 – 39)</td>
<td></td>
</tr>
<tr>
<td><strong>R situation</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>R0</td>
<td>11</td>
<td>100</td>
<td>83.3</td>
<td>27.78</td>
<td>(14 – 114)</td>
<td></td>
</tr>
<tr>
<td>R1</td>
<td>4</td>
<td>66.67</td>
<td>0</td>
<td>0</td>
<td>(5 – 20)</td>
<td></td>
</tr>
<tr>
<td>R2</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>12</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Clear histologically margins</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.001*</td>
</tr>
<tr>
<td>Yes</td>
<td>11</td>
<td>100</td>
<td>83.33</td>
<td>27.78</td>
<td>(14 – 114)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>5</td>
<td>37.5</td>
<td>0</td>
<td>0</td>
<td>(5 – 20)</td>
<td></td>
</tr>
<tr>
<td><strong>Adjuvant therapy</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.056</td>
</tr>
<tr>
<td>No</td>
<td>8</td>
<td>71.43</td>
<td>47.62</td>
<td>-</td>
<td>(5 – 24)</td>
<td></td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>5</td>
<td>100</td>
<td>66.67</td>
<td>0</td>
<td>(11 – 39)</td>
<td></td>
</tr>
<tr>
<td>Chemotherapy+Radiation b</td>
<td>3</td>
<td>100</td>
<td>100</td>
<td>0</td>
<td>(30 – 114)</td>
<td></td>
</tr>
<tr>
<td><strong>Surgery</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.856</td>
</tr>
<tr>
<td>Local excision</td>
<td>11</td>
<td>80</td>
<td>66.67</td>
<td>33.33</td>
<td>(5 – 114)</td>
<td></td>
</tr>
<tr>
<td>Hepatectomy</td>
<td>5</td>
<td>100</td>
<td>66.67</td>
<td>0</td>
<td>(11 – 38)</td>
<td></td>
</tr>
</tbody>
</table>

a Log-rank test, b No deaths, c Comparing only R0 vs. R1

According to tumor histology the median survival was significantly higher in patients with nodular or papillary macroscopic appearance than in patients with infiltrating macroscopic appearance (median: 38 vs. 27 months, p=0.049, Fig.4). None of the patients with a good histology died and the median survival of patients with moderate histology was 38 months, while the median survival of patients with poor histology was 20 months (p=0.046). There was a trend showing that patients with adjuvant therapy had a better survival than patients with no adjuvant therapy (p=0.056). In fact, none of the three patients that had the combination therapy of chemotherapy and radiation died.

Discussion

Altemeier-Klatskin’s tumor is an uncommon malignancy with a relatively poor prognosis providing a major therapeutic challenge. Surgery remains the only intervention offering the possibility of cure (16). In the present series, the resectability rate was 43.2%, while there was a 7.4% operative mortality and 37.5% postoperative morbidity. The median survival of patients undergoing resection was significantly higher than patients undergoing no resection. Furthermore, patients with R0 resection experienced significantly superior survival than patients with R1 resection. These results showed a high resectability rate, low operative mortality, and improved long-term survival compared to that achieved by palliative surgery. Apparently, these findings are not surprising, and are consistent with prior similar investigations (3,7, 21,22).

Over the last two decades, advances in hepatic surgery have led to a more aggressive approach to hilar cholangiocarcinoma. Particularly, liver resection was added to biliary resection to treat tumors with direct hepatic invasion, as well as to obtain clear histological margins on carcinomas.
that frequently extend longitudinally to the hepatic ducts (7,8,23). Lately, the majority of hepatobiliary surgeons appear to agree with the concept of concomitant hepatectomy, when performing resectional surgery for hilar bile duct cancer, in terms of both obtaining a negative resection margin and increasing the number of resectable patients (7,8,11,24). Launois et al (3) claimed that the indication for an associated hepatectomy depends on two factors; tumor location and TNM classification. If tumor location is type I or II, if primary tumor is Tis or T1, and in stage 0 or stage I tumors, tumor resection alone is sufficient. In these cases, Mizumoto et al (25) reported that it might be preferable to combine tumor resection with resection of the caudate lobe. Moreover, if tumor location is type III or IV, or if the primary tumor is T2 or T3, and in stage II, III, or IV tumors, hepatectomy is necessary for achieving cure. Liver resection is especially indicated in case of invasion of a vascular structure, of distal tumor spread along the intrahepatic bile duct, and of unilobar metastatic tumor deposits on the liver surface (3).

In the present series, we performed local hilar resection for Bismuth-Corlette type I and II tumors, while caudate lobe was also resected in cases of posterior infiltration by the tumor into the liver parenchyma. For type III tumors hilar resection was carried out in combination with hemihepatectomy and caudate lobe resection. Recently published data, however, support a more aggressive approach that includes extended right hemihepatectomy/ caudate lobectomy for all patients with Bismuth-Corlette types I, II, IIIa and IV tumors, and left hemihepatectomy/ caudate lobectomy for those with Bismuth-Corlette type IIIb (26). Nevertheless, consensus does not appear to have been reached regarding the type of hepatectomy that should be performed and the type of patients in whom hepatectomy is indicated. Apparently, aggressive surgical approach for the treatment of hilar cholangiocarcinoma, which results in a significant survival benefit, does not come without cost. In our series, overall 6 (37.5%) patients suffered some form of perioperative complication. Nevertheless, these complications were managed without surgical intervention.

Extended hepatectomy for the treatment of hilar cholangiocarcinoma, in the setting of biliary obstruction and elevated bilirubin, can be associated with increased operative risk (27,28). To reduce the risks, several investigators emphasize the value of preoperative biliary drainage. This approach however remains very controversial. It is well known that the presence of preoperative biliary drainage increases biliary tree bacterial colonization and consequently can lead to life-threatening perioperative infectious complications (9). Conversely, several studies reported a reduced incidence of liver failure when preoperative biliary drainage was used (26,29). In this study, preoperative biliary drainage was performed in 14 patients by percutaneous transhepatic drainage and in one using an endoscopic insertion of two Amsterdam type stents, in order to decrease the operative risk of a major surgical procedure. These patients underwent preoperative biliary drainage with the surgeon’s consent. Although the benefit of preoperative biliary drainage is still debatable, we consider optimal preoperative drainage a prerequisite in patients who are about to undergo major liver resections and rely heavily on the functional reserve of the liver remnant after surgery.

In this study the presence of an R0 resection proved to be predictive of an improvement in survival. Indeed, patients with R0 resection experienced significantly longer survival than patients with R1 resection. Correspondingly, patients with histologically clear margins had significantly greater survival than patients with positive margins. These data emphasize the need for obtaining tumor-free margins.

Patients who had lymph node involvement showed worse survival (statistically not significant). The literature provides conflicting results regarding the association of lymph node status with survival, with some authors showing a clear effect (29,30) and some showing none (9,31).
study, there was no significant difference in survival according to Bismuth-Corlette type lesions and TNM staging or classification. Although several studies showed that survival depends on the stage of the disease (3,7,9), our data indicate that TNM staging and/or classification does not influence survival provided that a potentially margin-free resection can be offered. Similarly, there was no significant difference in survival according to the type of surgery. This suggests that the type of surgery does not influence survival as long as a margin-free resection can be offered. Hepatic resection should be added to biliary resection to treat tumors with direct hepatic invasion, as well as to obtain clear histological margins.

In this study, resections resulting in cancer-positive margins did not portend a survival benefit. Although Kawasaki et al (26) and Zervos et al (22) reported that even with cancer-positive margins, patients undergoing resection for hilar cholangiocarcinoma showed a survival advantage, the majority of investigators report no benefit for resections performed with positive margins (9,31). With reference to the above, we certainly would not advocate performing resections for Altemeier-Klatskin tumor with anything other than the intent to perform a R0 resection.

The median survival in patients with nodular or papillary macroscopic appearance was higher than in patients with infiltrating macroscopic appearance. The disappointing outcome in patients with infiltrating type has to be correlated with a more aggressive biological behaviour of this type of tumor (32). Notwithstanding this, we believe that R0 resection must be performed also in these type of tumors. In addition, none of the patients with a good histology died and the median survival of patients with moderate histology was longer than of patients with poor histology. Nevertheless, several investigators found that the degree of tumor differentiation does not significantly correlate with overall survival (3,33).

The effect of adjuvant chemotherapy and radiation on survival of patients with hilar cholangiocarcinoma remains inconclusive (34). Particularly, there are no properly conducted trials that provide evidence for a benefit of adjuvant radiotherapy. In spite of this, several investigators reported varying degrees of success with radiation therapy, either by external beam or brachytherapy in the treatment of cholangiocarcinoma (35,36). In contrast, Pitt et al showed that adjuvant external beam radiotherapy did not have an effect on survival in patients with localized perihilar cholangiocarcinoma, in either resected or palliatively treated patients (37). On the other hand, Todoroki et al (38) found that the combination of intraoperative and postoperative radiotherapy, when applied to patients with microscopic tumor residue, led to favorable outcomes. In our series, patients with adjuvant therapy had a better survival than patients with no adjuvant therapy. The results of this study are consistent with the findings of larger similar studies, nevertheless they should be interpreted with caution because of the small sample size.

In conclusion, negative surgical margins, tumor differentiation and infiltrating macroscopic appearance, were statistically significant prognostic factors. Our findings emphasize that complete resection of the tumor with negative histopathological margins offers the best possibility of long-term survival, and that the addition of hepatectomy to biliary resection results in a greater number of patients with negative margin resections.

**Conflicts of interest**

None to declare.

**References**


