Carcinoma of the ampulla of Vater: prognostic factors after curative surgery: a series of 45 cases

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Abstract

Background—Some adjuvant or neo-
adjuvant therapy could be important for
patients operated on for tumours of the
ampulla of Vater, especially for those
having a higher risk of recurrence.

Aim—To evaluate prognostic factors after
curative surgery based on a series of 45
cases of malignant tumours of the Oddi
sphincter.

Patients—From 1970 to 1992, a curative
resection was performed in 45 patients
(age 62.8 (SD 10.1) years) with adeno-
carcinoma of the ampulla. Surgical
procedures included pancreatoduden-
ectomy (n=42) and resection of the
ampulla (n=3). Actuarial survival was 44
(SD 9)% at five years.

Methods—Various prognostic variables
were studied: clinical manifestations,
macroscopic aspect, differentiation, non-
invasive adenomatous component, mucin
histochemistry, immunohistochemistry
(CEA, CA19.9, p53, Ki67), and accepted
classifications (Blumgart and Kennedy,
Martin, Yamaguchi and Enjoji, Talbot
et al, pTNM).

Results—Variables with prognostic power,
in order of importance were: Classification
of Talbot et al; CA19.9; pTNM; sialomucins;
classification of Yamaguchi and Enjoji;
Martin classification; sulphomucins; non-
invasive adenomatous component (positive>negative); jaundice; tumour localisation.

Conclusions—This series confirmed the
prognostic power of former classifications
and showed the prognostic power of other
variables (mucin, non-invasive adeno-
matous component, CA19.9).

Keywords: ampulla of Vater, carcinoma, surgery,
immunohistochemistry, p53.

Primary malignant tumours rarely occur in
the ampulla of Vater. Pancreatoduden-
ectomy with or without resection of the pylorus is the
procedure of choice. Prognosis is radically
different from tumours of the head of the
pancreas as five year survival after complete
surgical resection is 30% to 60%. Several
adjuvant postoperative treatments have been
proposed in an attempt to improve survival
rates. Splinter et al did not find any improve-
ment in three year survival after chemotherapy.
Willet et al proposed postoperative ir-
radiation with or without 5-fluorouracil for
their patients and noted a reduction in the rate
of local recurrence but no beneficial effect on
survival. A recent randomised controlled study
in Scandinavia showed a significant improve-
ment in mean overall survival and in two year
survival after postoperative chemotherapy in
patients undergoing curative surgery for cancer
of the head of the pancreas or the papilla
(14/61 cases). The implications of these results
are, however, subject to discussion as the series
were either non-randomised, or included only
a few patients, or reported cancer of the
pancreas and the papilla together. In addition,
as for adenocarcinoma of the colon, the
rationale for treating all patients undergoing
what is considered to be a curative surgical
procedure is not always clear. A more appro-
priate approach would be to reserve adjuvant
therapy for patients at higher risk of recur-
rence. There are indeed several classifi-
cations aimed at predicting prognosis. More
recently, certain criteria based on histo-
chemistry (mucin typing) or immunohisto-
chemistry (CEA, C19.9, Ki67, or p53) have
been useful for other types of tumours. In this
retrospective study we evaluated clinical, histo-
logical, histochemical, and immunohisto-
chemical criteria of prognosis with special
focus on recent histochemical or immuno-
logical labelling, in patients who underwent
curative surgery for tumours of the ampulla of
Vater.

Methods

Between 1 January 1970 and 31 December
1992 curative surgery was performed on 45
patients for primary malignant tumours of the
ampulla of Vater and histologically demon-
strated invasion of the basal membrane.
Patients who were treated with a palliative
procedure (as defined operatively) or had
invaded margins (in the pathology report) and
those who had an in situ lesion or dysplasia
were excluded from the study.

Age, sex, signs leading to diagnosis (jaundice,
pain, anaemia, bleeding), and preoperative
diagnostic findings were obtained from the hos-

cial records of the 45 patients. After surgery,
the macroscopic aspect of the tumour (vege-
tation, nodular, ulceration), the largest diameter,
and initial localisation (true tumour of the
ampulla, or tumour arising from periampullary
duodenal surface mucosa, from the common
duodenal duct, or pancreatic duct) were recorded.
All pathology slides were then reviewed prospect-
ively focusing on infiltration of the tumour,
Carcinoma of the ampulla of Vater: prognostic factors after curative surgery: a series of 45 cases

degree of malignancy, and differentiation according to the criteria of Von Dinges.

These data were used to assign patients in the following classifications: (1) initial and modified Blumgart and Kennedy classifications; (2) four stages in the classification of Martin \( ^6 \); stage I=vegetating tumour limited to the epithelium without involvement of the Oddi sphincter, stage II=tumour localised in the duodenal submucosa without involvement of the duodenal muscularis propria but possible involvement of the Oddi sphincter, stage III=tumour of the duodenal muscularis propria, stage IV=tumour of the periudodenal area or the pancreas with proximal or distal lymph node involvement; (3) Classification of Yamaguchi and Enjoji, \( ^7 \), very similar to the Martin classification; (4) Classification of Talbot et al \( ^8 \) associating an infiltration score (from 1 to 4 according to increasing degrees of infiltration) and a tumour differentiation score (from 1 to 3 for well, medium, and poorly differentiated tumours) giving a sum which separates the patients into group 1 with a sum from 2 to 4 and group 2 with a sum from 5 to 7; and (5) the pTnM classification, in which stages are defined as: T1=lesion limited to the ampulla, T2=invagination of the duodenal wall, T3=invagination of the pancreas extending less than 2 cm, and T4=invagination of the pancreas extending further than 2 cm, each patient is then assigned to stage I=T1N0, stage II=T2-3N0, stage III=T1-3N1, or stage IV=T4anyN.

Finally the presence or absence of an adenomatous component was identified according to the recent description by Yamauchi et al \( ^9 \) who determined that there is an adenomatous component if the glandular structures forming the adenomas lying near the carcinomas cover at least 20% of the total surface area of the tumour.

Evidence of mucin secretion and the type of mucin secreted was then prospectively obtained with PAS and Alcian blue staining at pH 2-5 to separate neutral and acid mucins. Acid mucins were then divided into sulphomucins and sialomucins with a combined high iron diamine and Alcian blue staining at pH 2-5. Results were expressed semiquantitatively as: no secretion=0, secretion by less than 50% of the tumour cells=+, and secretion by more than 50% of the tumour cells=++. Tumours with or without neutral mucin secretion and tumours with or without predominant secretion or sulphomucin and sialomucin (including cases with exclusive secretion of these types of mucins and cases with mixed and predominant secretion) were also identified for the prognostic study.

Four antibodies were used for the immunohistochemistry study: CEA, CA19.9, p53, and Ki67. Anti-CEA II7 monoclonal antibodies (Dako laboratories) specific for the Gold 1 epitope were used to detect CEA. Monoclonal TM clone (CisBioInternational, Saclay, France) was used to detect C19.9. Monoclonal DO7 (Dako laboratories) was used to detect p53 protein. Finally, an anti-Ki67 Mib1 clone (Immunotech laboratories) was used for Ki67.

Streptavidin-biotin coupled with peroxidase was used to label these four antibodies. Final detection was based on antigen-antibody reactions with colorimetric detecting using H2O2 and chromogenic 3,3 diaminobenzidine tetrahydrochloride (DAB). Anti-CEA and anti-CA19.9 immunolabelling were expressed semiquantitatively as: no labelling=0, labelling on at least one third of the tumour surface area=+, labelling of at least two thirds of the tumour surface area=++, and labelling of the entire tumour surface area=+++.

Labeling distribution was also noted as apical or diffuse. Results for anti-p53 and anti-Ki67 were determined as the mean of 10 fields with a \( \times \) 400 magnification. Results were expressed as percentage of labelled cells.

Statistical analysis

Mean (SD) was used to analyse quantitative variables. Kaplan-Meier curves were drawn to evaluate specific survivals and were compared using the log rank test or the generalised Wilcoxon test. For the two continuous variables, anti-p53 and anti-Ki67 labelling, the cut off point was set at 5% for p53 and at 15% for Ki67. The \( \chi^2 \) test and the exact Fisher test were used to analyse the association of several variables for prognostic value. Significance was set at 5%.

Results

Descriptive analysis

There were 45 patients – 25 men and 20 women, mean age 62.8 (SD 10.1) (range 13–80) years. The youngest patient was a women with familial adenomatous polyposis (the only patient with a similar clinical situation in this study). The most frequent clinical signs were jaundice (n=32, 71%), abdominal pain (n=26, 58%), anaemia (n=9, 20%), and haemorrhage (n=5, 11%). The delay between onset of symptoms and diagnosis was short (3 (SD 2-8) months). Weight loss was noted in 51% of the cases. Preoperative endoscopical biopsies were obtained for 29 patients and were positive in 23 (80%). Pancreatoduodenectomy was performed in 37 cases (82%), pancreatoduodenectomy with resection of the entire pancreas in five cases (11%), and ampullectomy alone in three cases (7%). Three patients (6-7%) died during the immediate postoperative period and overall postoperative morbidity was 22% (three haemorrhages, three major infections, two abscesses, and one case each of respiratory complications and ulceration of the anastomosis).

Macroscopically the tumours measured 2-5 (SD 1-9) cm in diameter. There were 21 vegetating tumours (47%), 14 nodular tumours (31%), and 10 ulcerated tumours (22%). Strictly ampullary localisation was seen in 28 cases (62%). Other localisations were: lower end (within the Oddi sphincter and ampulla) of the common bile duct (n=5, 11%); end (within the Oddi sphincter and ampulla) of the pancreatic duct alone (n=1); periampullary
survival a neutral mucins in weak in years

**TABLE I**

<table>
<thead>
<tr>
<th>Classification</th>
<th>Patients n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blumgart and Kennedy&lt;sup&gt;i&lt;/sup&gt;:</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>13 (29)</td>
</tr>
<tr>
<td>II</td>
<td>8 (18)</td>
</tr>
<tr>
<td>III</td>
<td>8 (18)</td>
</tr>
<tr>
<td>IV</td>
<td>4 (9)</td>
</tr>
<tr>
<td>III</td>
<td>12 (27)</td>
</tr>
<tr>
<td>Blumgart and Kennedy (modified):</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>7 (16)</td>
</tr>
<tr>
<td>II</td>
<td>19 (42)</td>
</tr>
<tr>
<td>III</td>
<td>19 (42)</td>
</tr>
<tr>
<td>Talbot et al&lt;sup&gt;ii&lt;/sup&gt;:</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>33 (73)</td>
</tr>
<tr>
<td>II</td>
<td>12 (27)</td>
</tr>
<tr>
<td>Martin&lt;sup&gt;iii&lt;/sup&gt;:</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>4 (9)</td>
</tr>
<tr>
<td>II</td>
<td>2 (4)</td>
</tr>
<tr>
<td>III</td>
<td>23 (51)</td>
</tr>
<tr>
<td>IV</td>
<td>16 (35)</td>
</tr>
<tr>
<td>Yamaguchi and Enjoji&lt;sup&gt;iv&lt;/sup&gt;:</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>4 (9)</td>
</tr>
<tr>
<td>II</td>
<td>2 (4)</td>
</tr>
<tr>
<td>III</td>
<td>25 (56)</td>
</tr>
<tr>
<td>IV</td>
<td>14 (31)</td>
</tr>
<tr>
<td>pTNM:</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>7 (16)</td>
</tr>
<tr>
<td>II</td>
<td>29 (64)</td>
</tr>
<tr>
<td>III</td>
<td>3 (7)</td>
</tr>
<tr>
<td>IV</td>
<td>6 (14)</td>
</tr>
</tbody>
</table>

**Prognostic factors**

Among the 22 factors studied, 11 were identified as having prognostic value. Table II gives their degree of significance and the five-year survival rate in each sub-group. A positive correlation between prognostic factors was found in five of the possible combinations:

**TABLE II**

<table>
<thead>
<tr>
<th>Variable value</th>
<th>Patients (n)</th>
<th>Survival rate (%) at 5 y</th>
<th>p Value</th>
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</thead>
<tbody>
<tr>
<td>Position of tumour:</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Ampulla</td>
<td>28</td>
<td>54</td>
<td>0.05</td>
</tr>
<tr>
<td>Other</td>
<td>17</td>
<td>32</td>
<td></td>
</tr>
<tr>
<td>Site of CA19.9 labelling:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Apical</td>
<td>9</td>
<td>88</td>
<td>0.04</td>
</tr>
<tr>
<td>Cytoplasmic</td>
<td>34</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td>Jaundice</td>
<td>13</td>
<td>75</td>
<td>0.04</td>
</tr>
<tr>
<td>Yes</td>
<td>32</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td>Non-invasive adenomatous component:</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>16</td>
<td>68</td>
<td>0.03</td>
</tr>
<tr>
<td>No</td>
<td>29</td>
<td>27</td>
<td></td>
</tr>
<tr>
<td>Sulphomucin secretion:</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>34</td>
<td>58</td>
<td>0.02</td>
</tr>
<tr>
<td>Yes</td>
<td>11</td>
<td>32</td>
<td></td>
</tr>
<tr>
<td>Martin classification:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I + II</td>
<td>6</td>
<td>100</td>
<td>0.02</td>
</tr>
<tr>
<td>III + IV</td>
<td>39</td>
<td>35</td>
<td></td>
</tr>
<tr>
<td>Yamaguchi and Enjoji classification:</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>I + 2</td>
<td>6</td>
<td>100</td>
<td>0.02</td>
</tr>
<tr>
<td>I + 4</td>
<td>39</td>
<td>35</td>
<td></td>
</tr>
<tr>
<td>SiAlomucin secretion:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>23</td>
<td>100</td>
<td>0.007</td>
</tr>
<tr>
<td>No</td>
<td>22</td>
<td>27</td>
<td></td>
</tr>
<tr>
<td>pTNM:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 + II</td>
<td>36</td>
<td>55</td>
<td>0.003</td>
</tr>
<tr>
<td>III + IV</td>
<td>9</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>CA19.9 intensity:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-1</td>
<td>13</td>
<td>92</td>
<td>0.002</td>
</tr>
<tr>
<td>++ - +++</td>
<td>32</td>
<td>24</td>
<td></td>
</tr>
<tr>
<td>Talbot et al classification:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>33</td>
<td>57</td>
<td>0.001</td>
</tr>
<tr>
<td>II</td>
<td>12</td>
<td>10</td>
<td></td>
</tr>
</tbody>
</table>
Carcinoma of the ampulla of Vater: prognostic factors after curative surgery: a series of 45 cases

Early in our series we performed local resection in three cases. One patient had to be re-operated on for haemorrhage and the tumour recurred in all three patients. Pancreatoduodenectomy is well tolerated as confirmed by the outcome in this series (mortality=6.7%, morbidity=22%).

Multivariate analysis could not be performed due to the few patients and deaths (n=24) in this series. However, data for 22 variables were analysed and 11 were found to have prognostic value. Among these there were five combinations showing correlations between two variables (exact Fisher test or \( \chi^2 \) test).

Neither age of the patients (> or ≤60 years) nor sex had an effect on prognosis. However, all of the early deaths (immediate postoperative period or within six months of surgery) occurred in patients over 60. The only clinical variable tested, jaundice, was found to have an unfavourable effect on prognosis. This finding, also reported by several other authors,15 18 is related to the fact that jaundice is an expression of spread of disease14 just as is the association we found between the presence of jaundice and a more severe stage in the Martin classification.

Among the other macroscopic variables studied, neither tumour size nor the macroscopic aspect (vegetative, nodular, or ulceration) had prognostic value. Previous reports are contradictory.12 15 19–22 The macroscopic histological classifications initially described by Blumgart and Kennedy6 and then modified by Martin,6 did not isolate any differences in prognosis. This may be related to the rather subjective nature of these classifications. The other macroscopic criterion examined, tumour localisation, was found to affect prognosis as tumours strictly limited to the ampulla had a better prognosis. This has previously been reported.11 23 Tumours which originate at the sphincter end of the pancreatic duct seem to have poor prognosis.11 It may, however, be difficult to distinguish the point of origin of extended tumours, and an analysis of mucin secretion can provide interesting results11 because different sets of tissues secrete different mucins. Neoplasia is, however, usually associated with a modification in mucin secretion which in itself may have prognostic power.

Most of the variables which had prognostic value were those distinguished by histology or histochemical or immunohistochemical methods. In this series, a non-invasive adenomatous component was associated with better prognosis. Adenomatous residues are often found within tumours of the ampulla18 21 confirming the fact that adenomas of the papilla are precancerous lesions, a finding which would be collaborated by the demonstration of increasing immunoreactivity to CEA and CA19.9 with increasing degrees of dysplasia.14 Adopting the criteria of Yamauchi et al to define the presence of adenomatous residues may be too restrictive, but the use of a cut off value (20%) permits the differentiation of cases in which residues are important from those in which the area involved is minor intensity and localisation of CA19.9 immunolabelling, non-invasive adenomatous component and the classification of Talbot et al,3 sialomucin secretion and Martin classification, classifications of Martin and Yamaguchi and Enjoji,7 and jaundice and the Martin classification. Eleven factors had no prognostic value: age (≤ or >60 years), sex, macroscopic aspect (vegetative, nodular, ulceration), tumour size, initial and modified Blumgart and Kennedy classifications, neutral mucin secretion (presence or absence), intensity and localisation of CEA labelling (apical, cytoplasmic), p53 labelling (positive, negative), and Ki67 labelling (positive, negative).

Discussion

This retrospective study of primary carcinomas of the ampulla of Vater showed that several factors have prognostic value. Some are well known, others are formerly unreported factors (CEA immunolabelling, mucin histochemistry, non-invasive adenomatous component).

This series confirms the exceptional nature of malignant tumour of the Vater ampulla as curative surgery was performed in only 45 cases over a 22 year period. During this same period, 22 other patients were also operated on for ampullary tumours: 14 underwent palliative surgery and eight were cured of dysplasia or in situ carcinoma of the ampulla of Vater. The rationale for not including patients who had undergone palliative surgery was that the aim was to determine whether adjuvant or neoadjuvant treatments could be usefully proposed for patients with resectable tumours. The exclusion of non-invasive in situ tumours and dysplasias was motivated by the fact that such histological forms would not lead to the prescription of a complementary medical treatment.

The descriptive data obtained in this series are similar to those reported in the medical literature10–15: mean age slightly over 60 years, slight male predominance, and frequent jaundice, pain, and haemorrhage. Survival at five years in our patients was 44 (SD 7)% which is high compared with that reported in the literature despite the exclusion of in situ tumours from the analysis. Preoperative endoscopic exploration, performed in 29 of our patients, gave the diagnosis of malignancy in 80%. This is close to the diagnostic yield of endoscopic biopsies reported in one Japanese series,16 in which positive pathology results were obtained in 70%. To improve endoscopic diagnosis, other endoscopic techniques, including biopsy after endoscopic sphincterotomy or snare biopsies,17 may be indicated.

Pancreatectoduodenectomy is the treatment of choice for tumours of the ampulla of Vater. Local procedures such as simple ampullectomy have been proposed to reduce operative mortality. In a recent review, Allema et al12 reported lower mortality (6%) and a better five year survival rate (47%) for ampullectomy than for pancreatectoduodenectomy (12%–35%).

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or absent. There are two possible explanations as to why some cancers of the ampulla have no detectable adenomatous component. Either tumoural extension has already destroyed the adenomatous tissue or certain cancers develop without going through an adenoma stage. Such adenomatous residues are described in about one third of the cases of cancer of the colon and have a frequency inversely proportional to tumour size. Such an association has been suggested for tumours of the papilla but in two recently reported series, there was a considerable difference in prognosis for tumours with a non-invasive adenomatous component. Such tumours showed a better prognosis (five year survival 78 and 75% v 22 and 11% in the series of Yamaguchi et al and 68% v 27% in ours). It could thus be hypothesised that tumours without a non-invasive adenomatous component correspond to aggressive tumours with a rapid progression destroying the adenomatous tissue or to new tumours of the ampulla which have not gone through an adenoma stage; both cases would have a particularly severe prognosis. We also showed an association between the presence of a non-invasive adenomatous component and the Talbot classification, which takes into consideration both tumour infiltration and differentiation. This suggests that these tumours would also be less well differentiated. The four histology classifications examined here (Martin, Yamaguchi and Enjoji, pTNM, and Talbot et al) all had prognostic power but because of the few patients, several stages had to be grouped together to show significance. These expected conclusions validate the equality of the other results. The classifications of Martin and Yamaguchi and Enjoji are similar and, as for the pTNM classification, are essentially based on tumour infiltration. Most studies have found that tumour infiltration has prognostic power, especially in patients with pancreatic and lymph node involvement. and the degree of tumour infiltration and on the degree of tumour differentiation would seem to provide promising information. In our series, it produced the most discriminating classification. For most of the authors, and tumour differentiation affects prognosis and as the classification of Talbot et al uses both criteria for tumour infiltration and more cytological criteria (differentiation of cell architecture, cell differentiation, number of mitoses) it gives a better expression of the tumour cell status. Recent progress in genetics has shown that such cellular criteria sometimes have more prognostic power than clinical or histological criteria.

Histologically, the tissues in and around the Oddi sphincter are highly complex. There are four types of mucosa, each with a different pattern of secretion of mucus. In addition, it has been shown that neoplastic development in the gut is often associated with a modification in mucin production. Such modifications have also been suggested for cancers of the papilla. The effect of tumorous mucin secretion on prognosis has only recently been approached. In a complete histochemical study, Dawson et al. were able to divide acid mucins into sulphomucins and sialoglycans and show that prognosis of intra-ampullary tumours varies with the type of mucin secreted. Tumours secreting sialoglycans would have a better prognosis. Our findings would favour this hypothesis as the better prognosis was found in tumours with predominant sialoglycan secretion and in tumours without predominant sulphomucin secretion.

We also analysed CEA, CA19.9, Ki67, and p53 expression using immunohistochemistry. The only effect on prognosis found was for CA19.9, which seemed to have an unfavourable influence both for labelling intensity and localisation, which were associated. For certain authors, apical labelling is not an entity, rather it corresponds to weaker labelling than diffuse cytoplasmic labelling. The poor prognosis of CA19.9 positive cancers of the ampulla of Vater has been noted previously. Whether this unfavourable affect is an independent factor or simply related to the effect of other factors remains to be determined. Nakao et al. reported that intense label uptake was seen in patients with pancreatic involvement. Conversely, Kamisawa et al. found that immunolabelling was negative in all tumours located in the ampulla. Despite the larger number of tumours in our series, we were unable to show any such association. We were unable to show any prognostic power for CEA, a finding which would not support the suggestion by Kamisawa et al. that CEA has real, though weaker prognostic power than CA19.9. We have no explanation for these conflicting findings. Likewise, neither p53 nor Ki67 had any effect on prognosis in our series. We found that p53 protein had accumulated in 49% of our cases. This is similar to the rates reported in two other series showing p53 positive results in five out of nine tumours of the ampulla of Vater and in 66% of ampullary and common bile duct tumours. The unfavourable prognosis associated with such labelling in other tumours, notably in tumours of the oesophagus, has not been searched for previously in tumours of the ampulla of Vater. However, in a series of malignant tumours of the bile ducts and ampulla, Teh et al. found that, unlike other organs of the gall bladder, there was no association between the low degree of differentiation and p53 positivity (a finding which may be related to the lack of prognostic value for p53 found here). Finally, we were unable to show any prognostic value for Ki67 immureactivity. Other more recent studies have, however, been able to confirm this finding in colorectal cancer.

In conclusion, the findings in this series of 45 tumours of the ampulla of Vater treated by curative resection showed that 11 factors were significantly correlated with survival rate. Among these factors, jaundice and tumour localisation are well known for their prognostic
Carcinoma of the ampulla of Vater: prognostic factors after curative surgery: a series of 45 cases

power. For several others such as the histo-
prognostic classifications (Martin, Yamaguchi and Enjoji, Talbot et al, pTNM) there is a
logical explanation for the relation with outcome. Other factors such as the type of mucin secreted, the presence of a non-invasive adenomatous component, and CA19.9 mucin have been less well known. Some of these variables (mucin secretion, CA19.9 immunoreactivity on endoscopic biopsies) or even depth of extension (using echoendoscopy or echolaraporoscopy), can be determined preoperatively and would therefore lead to the use of a neoadjuvant treatment. All these factors can also be evaluated postoperatively to determine whether adjuvant treatment is indicated. The aim of such adjuvant therapy would be to increase five year survival further by treating patients with factors of poor prognosis. For example, based on factors showing the highest level of significance in our series, the prognosis can be determined with further precision if two factors are associated. Thus for patients in stage 1 in the classification of Talbot et al, an assessment of sulphomucin secretion can identify non-secretors, who have a good prognosis (100% survival at five years) and secretors with poor prognosis (41% survival at five years). Likewise, CA19.9 immunoreactivity can distinguish between patients with good prognosis (CA19.9 negativity, five year survival 100%) and those with poor prognosis (CA19.9 positivity, five year survival 36%). However, this retrospective series with few patients can only provide tentative conclusions which must be validated in a prospective study. If validated, these findings could lead to clinical trials of adjuvant therapy proposed on the basis of histoprognosis.

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