

Primary hepatic malignancy: the role of liver transplantation

Between January 1982 and April 1989, 134 patients with a suspected liver neoplasm were referred to the liver unit, Queen Elizabeth Hospital, Birmingham. In 105 (78 per cent), a primary hepatic neoplasm was histologically confirmed, and 47 patients (45 per cent) proved to have primary hepatocellular carcinoma. Twenty-nine orthotopic liver transplants were performed in 28 of these patients (27 per cent). Twenty patients (71 per cent) survived 30 days or longer (median 11.5 months; range 2-87 months), of whom nine are currently alive. We retrospectively analysed our data to determine the influence of preoperative evaluation, histological type and staging on outcome. Computed tomography proved to be superior to intraoperative assessment (86 versus 58 per cent) in diagnosing tumour positive nodes. Patients with tumour negative lymphadenopathy had a better prognosis. Postoperative stage I/II had a median survival of 16 months (range 3-87 months) compared with 7.5 months (range 2-20 months) for stage III. Non-cirrhotic patients with hepatocellular carcinoma had the best prognosis; cholangiocellular carcinoma and cirrhotic patients with hepatocellular carcinoma had the worst outcome with no survivors beyond 1 year. Because of the advanced stage of disease at the time of presentation, the value of liver transplantation in primary liver cancer is limited. For those presenting with advanced disease confined to the liver (stage I/II) in whom conventional hepatic resection is not possible, significant benefit can be achieved in selected cases.

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Complete surgical excision represents the only chance of cure for patients with primary liver malignancy. The presence of advanced cirrhosis or multifocal hepatic malignant disease means that only a small proportion of patients will be offered an attempt at segmental resection and, of these, approximately 30 per cent will survive 5 years¹. In 1967 in Denver, Starzl *et al.* performed the first orthotopic liver transplant (OLT) for hepatocellular carcinoma on an 18-month-old girl who survived 13 months². Since then, many other patients with primary hepatic malignancy have undergone total hepatectomy and liver replacement in an effort to clear all malignancy.

Disappointing results, largely due to the high incidence of tumour recurrence, led several centres to discontinue liver grafting for primary tumours³ but some of the longest survivors have been transplanted for this indication⁴⁻⁶. Because of the difficulties in assessing the extent of nodal involvement with tumour or tumour extension at the time of surgery, an approach based on detailed preoperative assessment to detect extrahepatic spread and thus stage the disease, has been advocated⁵.

We have analysed our own experience and attempted to determine the accuracy of both preoperative and intraoperative assessment of disease and to correlate stage of disease with patient outcome following liver transplantation.

Patients and methods

Between January 1982 and April 1989, 134 patients with suspected liver neoplasm were referred to the Liver Unit, Queen Elizabeth Hospital, Birmingham (Table 1). In 105 patients a diagnosis of primary liver tumour was confirmed histologically. Twenty patients of 47 with hepatocellular carcinoma were excluded from the analysis (advanced disease and not offered a transplant, died during assessment or while waiting for a liver graft) and six others had an exploratory laparotomy (two underwent liver resection, one had a palliative biliary drainage procedure and three were inoperable). The remaining 21 patients, 15

with hepatocellular carcinoma and six patients with the fibrolamellar variety underwent OLT. Transplantation was also performed in three of 42 patients (one incidental) with central cholangiocellular carcinoma and in four of 16 patients with tumours of mesenchymal origin.

Primary hepatic malignancy was the main indication for liver transplantation in 22 patients. Six patients had liver replacement primarily to treat end-stage cirrhotic liver disease and were found to have a coincidental tumour either before transplantation or at histological examination of the excised liver. All patients underwent preoperative assessment to detect the extent of disease⁴.

A total of 29 grafts was performed in 28 patients (15 male) with a mean age 38.5 years; range 3-65 (Table 2). Operative technique and immunosuppression has been previously reported⁴ with the exception of venovenous bypass⁷, recently used in selected cases. Abnormal radiological appearance of lymph nodes on preoperative scan in the

Table 1 Histological classification of liver tumours

Histological diagnosis	Number of patients (n = 134)	Number transplanted
Hepatocellular carcinoma		
Non-fibrolamellar	40	15 (53.6)
Fibrolamellar	7	6 (21.4)
Cholangiocellular carcinoma	42	3 (10.7)
Mesenchymal tumours	16	4 (14.3)
Giant cavernous haemangioma	5	
Epithelioid haemangioendothelioma	2	(1)
Infantile haemangioendothelioma	1	(1)
Angiosarcoma	5	(2)
Leiomyosarcoma	2	
Spindle cell tumour	1	
Metastatic	29	

Numbers in parentheses are percentages of the total numbers

Table 2 Orthotopic liver transplantation (OLT) for primary hepatic malignancy

OLT number	Age	Sex	Tumour type	CT +ve	IO +ve	HIST +ve	Size (cm)	CE	Survival (months)	Cause of death
Cirrhotic										
1	54	F	NF HCC	n.a.	Y	N	11	Y	0	Sepsis
6	55	M	NF HCC	n.a.	N	N	m.f.	Y	0	Infarction
9	13	M	NF HCC	N	N	Y	m.f.	N	2	Recurrence
48	59	M	NF HCC	N	Y	N	10	Y	12	Recurrence
60/62	56	M	NF HCC	N	Y	N	1	Y	0	Bleed
78	22	F	NF HCC	N	N	N	1.5	Y	0	Rejection, necrosis
79	45	M	NF HCC	N	N	N	m.f.	Y	0	Bleed
117	46	M	NF HCC	N	N	N	m.f.	Y	3	Hepatitis B recurrence
119	55	M	NF HCC	N	N	N	m.f.	Y	0	MOF
126	65	M	NF HCC	N	Y	N	m.f.	Y	0	Bleed
Non-cirrhotic										
2	39	M	NF HCC	n.a.	Y	N	22	Y	87	
5	44	M	NF HCC	N	Y	Y	m.f.	N	6	Recurrence
7	60	F	NF HCC	N	N	N	16	Y	71	
146	49	M	NF HCC	Y	N	N	15	Y	13	Recurrence
226	38	F	NF HCC	N	N	N	m.f.	N	5	
25	21	M	FL HCC	Y	Y	Y	15	N	18	Recurrence
28	27	F	FL HCC	N	Y	Y	15	N	0	Bleed
32	19	F	FL HCC	N	Y	N	18	N	20	Recurrence
70	23	F	FL HCC	N	N	N	16	Y	34	
131	21	F	FL HCC	N	Y	N	16	Y	19	
214	18	M	FL HCC	Y	Y	Y	18	N	8	
16	47	F	EHE	N	N	N	m.f.	Y	55	
39	53	F	CholCa	Y	Y	Y	m.f.	N	12	Recurrence
43	46	F	CholCa	Y	Y	Y	m.f.	N	11	Recurrence
65	33	F	AS	Y	Y	Y	m.f.	N	5	? recurrence
139	40	M	CholCa	Y	N	N	m.f.	N	7	Recurrence
237	37	M	AS	N	N	N	m.f.	Y	4	
241	3	F	IHE	N	N	N	20	Y	4	

Three patients were node negative but had incomplete excision of tumour (OLT 32 and 226 had tumour in the portal vein, OLT 139 had tumour in the extrahepatic bile duct). OLT 60/62 had a second liver graft 1 month after the first transplant. CT/IO/HIST relate to presence (Y) or absence (N) of enlarged nodes on computed tomography (CT) and intraoperatively (IO) and to tumour positive nodes at postoperative histology (HIST). n.a., not available; m.f., multifocal; CE, complete excision; MOF, multiorgan failure; NF HCC, non-fibrolamellar hepatocellular carcinoma; FL HCC, fibrolamellar hepatocellular carcinoma; CholCa, cholangiocellular carcinoma; AS, angiosarcoma; EHE, epithelioid haemangioendothelioma; IHE, infantile haemangioendothelioma

porta hepatis and coeliac axis was not considered an absolute contraindication to transplantation. These patients were subsequently defined as computed tomography (CT) positive for the purpose of this study. Any patient with lymph nodes that appeared macroscopically 'abnormal' intraoperatively (IO) was defined as IO-positive. Microscopic tumour in one or more nodes in the resected specimen was defined as histology (HIST) positive.

Lymph node status and stage of disease (Fortner Classification⁸) were correlated with outcome. The latter is a postoperative clinicopathological staging method. In this study stage II denotes a tumour confined to the liver but not amenable to complete excision by conventional techniques. CT scan and intraoperative macroscopic findings were compared with histology for their accuracy in determining node status.

Results

Non-fibrolamellar hepatocellular carcinoma

Fifteen patients (53 per cent) had non-fibrolamellar hepatocellular carcinoma (Table 2). In ten patients a diagnosis of hepatocellular carcinoma was made pretransplant. Two patients with hepatitis B, cirrhosis and raised α -fetoprotein levels were suspected of harboring a tumour but neither had preoperative histological or radiological confirmation. Three patients transplanted for chronic liver disease were found to have an incidental tumour on histological examination. Three of the five patients with occult neoplasm and five out of ten patients with preoperative histological diagnosis had multifocal tumour. In the unifocal group, the size of the occult tumours was 1 and 1.5 cm and, in those with a pretransplant diagnosis

of tumour, it ranged from 10 to 22 cm (mean 16 cm).

Seven (46 per cent) of these 15 patients, all with cirrhosis, died within 30 days of transplantation due to operative and postoperative bleeding (four), graft failure (two) and sepsis (one). Of the eight patients who survived the operation, three with hepatocellular carcinoma and cirrhosis (two positive for hepatitis B virus surface antigen) were dead at 1 year. One of these (OLT 117), with a raised serum α -fetoprotein level and positive for hepatitis B virus surface antigen but without preoperative histological confirmation of malignancy, had a multifocal tumour and was dead at 3 months with possible recurrence of hepatitis B infection (autopsy findings not available). Another patient (OLT 48) positive for hepatitis B virus surface antigen and with a 10 cm unifocal tumour, had complete resection but died at 12 months with bone metastases. Retransplantation was necessary in one patient (OLT 60/62; positive for hepatitis B virus surface antigen and cirrhosis) one month after the first graft because of hepatic artery thrombosis but died of perioperative bleeding.

Five patients had non-fibrolamellar hepatocellular carcinoma without associated cirrhosis. Two patients (OLT 5 and OLT 146) with a sclerosing variant of hepatocellular carcinoma associated with hypercalcaemia (4.9 and 2.8 mmol/l; normal range 2.2–2.6) and normal parathyroid hormone levels, developed hepatic recurrence with raised serum calcium levels and died at 6 and 13 months. Of the remaining three, one with multifocal tumour and incomplete excision (portal vein infiltration) is alive at 5 months and the other two (both unifocal) are alive at 71 and 87 months respectively.

Fibrolamellar hepatocellular carcinoma

Six (21 per cent) of the 28 patients transplanted had fibrolamellar hepatocellular carcinoma. The mean age of this group (four female) was 21.5 years (range 18–27 years) and tumour size ranged from 15 to 18 cm (mean 16 cm). Four had had a previous laparotomy with a view to resection that had proved possible in only one (OLT 70). One patient died after operation from bleeding.

Two died with recurrence at 18 and 20 months but both had incomplete resection, one with tumour positive nodes (OLT 25) and the other with portal vein infiltration (OLT 32). The disease free interval for the former patient was 6 months when he developed recurrence in the abdominal scar and lungs simultaneously. Despite chemotherapy he died 12 months later with tumour recurrence in the graft. The latter patient had a disease free interval of 16 months, developing recurrence in the abdomen and the grafted liver and died 4 months later (without chemotherapy).

One patient, OLT 70 (extended hepatic resection, 32 months pretransplant) was disease free from 24 months following a complete excision of the tumour at transplantation but developed metastases in the chest wall and local recurrence in the graft. This patient had chemotherapy and is alive with a good quality of life at 34 months post-transplant. The other two patients (one with metastatic lymphadenopathy) are alive and disease free at 8 and 19 months.

Other tumours

All three patients with cholangiocellular carcinoma had incomplete excision with multifocal tumour on histological examination, and died within 1 year from metastatic disease. One patient (OLT 39) was a therapeutic failure (sepsis, rejection recurrence) requiring hospitalization for most of her post-transplant life (12 months). Another patient (OLT 43) who previously had had a total colectomy and ileostomy did not pose any major technical problems during the transplant operation, had a disease free survival of 10 months. In the third patient (OLT 139), transplanted for primary sclerosing cholangitis, cholangiocellular carcinoma was an incidental finding. One of the two patients with angiosarcoma (OLT 65) died at 5 months with widespread intra-abdominal recurrence. The patient with epithelioid haemangioendothelioma (OLT 16; 47 years) was node negative and alive at 55 months. The 3-year-old patient (OLT 241) with infantile haemangioendothelioma was also node negative but with a 20 cm unifocal tumour and is alive and disease free at 4 months.

Prognostic factors and outcome

Twenty (71 per cent) patients survived 30 days or longer (median 11.5 months; range 2–84 months), of whom nine are currently alive.

Nodal assessment. The comparison between the three methods of evaluation of node status is shown in Table 3. The accuracy of normal and abnormal CT scan readings was 77 per cent and 86 per cent respectively.

Table 3 Accuracy of node status by CT scan, intraoperative assessment and histology

	Sensitivity (per cent)	Specificity (per cent)	Positive predictive value (per cent)	Negative predictive value (per cent)
CT +ve versus HIST +ve	67	91	86	77
IO +ve versus HIST +ve	58	55	58	55

CT +ve, computed tomography scan positive; HIST +ve, histology positive; IO +ve, intraoperative assessment positive

Table 4 Postoperative node status, Fortner stage and survival

Status	Patients (n)	Survival		
		Median (months)	Range (months)	Number alive
Node negative	13	13	3–87	8
Node positive	7	8	2–18	1
Stage I/II	10	16	3–87	7
Stage III	10	7.5	2–20	2

Table 5 Transplantation for primary hepatic malignancy

	Patients (n)	Survival		
		Median (months)	Range (months)	Number alive
Non-fibrolamellar hepatocellular carcinoma with cirrhosis	10	0	0–12	0
Non-fibrolamellar hepatocellular carcinoma without cirrhosis	5	13	5–87	3
Fibrolamellar hepatocellular carcinoma	6	18.5	0–34	3
Cholangiocarcinoma	3	11	7–12	0
Tumours of mesenchymal origin	4	15.5	3–55	3

Node status and staging. Eight patients died within 30 days of surgery. These patients were excluded because death was due to perioperative complications and unrelated to node status, completeness of excision or recurrent disease (four were stage I/II and four were stage III). Thirteen patients with no histological evidence of tumour in hilar nodes (but including three with local infiltration) had a median survival of 13 months (range 3–87 months) in contrast to those with microscopic tumour in the porta hepatis and coeliac nodes who had a median survival of 8 months (range 2–18 months), with no survivors beyond 18 months. Ten patients were classified as stage I/II, and ten as stage III (including three patients who had tumour infiltration of the portal vein/extrahepatic bile duct). The different survival for each stage is shown in Table 4.

Histological type. Cholangiocarcinoma and hepatocellular carcinoma with cirrhosis have the worst prognosis. The best outcome has been in the groups with non-fibrolamellar hepatocellular carcinoma without cirrhosis and fibrolamellar hepatocellular carcinoma (Table 5). The actuarial survival of patients with acute or chronic liver disease ($n=215$) and primary hepatic malignancy ($n=28$) after OLT is shown in Figure 1.

Discussion

The high recurrence rate, despite careful preoperative radiological and meticulous intraoperative evaluation, has led some groups to question the value of liver replacement as a curative therapy for primary liver malignancy⁵. In Europe, 635 patients have had an OLT for liver cancer, the majority for hepatocellular carcinoma (63 per cent). Three year survival rate ranges from 25 per cent for hepatocellular carcinoma to 18 per cent for secondary liver tumours⁹.

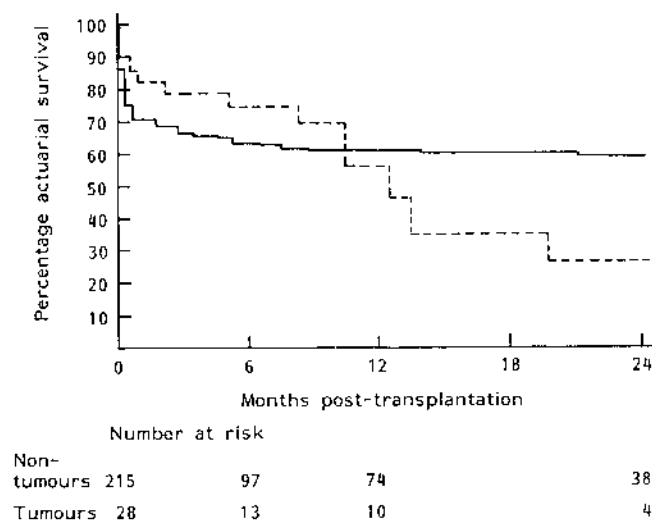


Figure 1 Actuarial survival of patients with acute or chronic parenchymal disease ($n=215$, —) and primary hepatic malignancy ($n=28$, ---) after orthotopic liver transplantation

Our data supports the concept that lymph node status is a prognostic factor in the long term survival of cancer patients following liver transplantation¹⁰. The Hannover group⁴ used a modified tumour nodes metastasis (TNM) staging system in their retrospective analysis of 95 liver recipients. Node negative patients (pN_0) with hepatocellular carcinoma had a 2 year actuarial survival rate of 36 per cent compared with no survivors beyond 1 year ($P<0.05$) in those with lymph node metastases (pN_1).

The accuracy of CT scanning to detect intrahepatic size of tumours is equivocal as reported by Mittal and colleagues¹¹. There is little published data on the accuracy of CT scanning in detecting metastatic lymphadenopathy in liver cancer. Imaging techniques such as CT scanning are inaccurate in detecting lesions <1.0 cm in diameter¹² and nodes with micrometastases may not be enlarged. CT scanning proved superior in sensitivity, specificity and accuracy of diagnosis compared with intraoperative findings. The accuracy of CT scanning in predicting tumour positive nodes is 86 per cent. Nevertheless, 23 per cent of patients undergoing transplantation will have tumour positive nodes despite a normal CT scan (Table 4). Nodes that appear abnormal to the surgeon at operation will, on histological examination, contain tumour deposits in 45 per cent of cases. Similar data on the inaccuracy of intraoperative assessment of lymph node involvement in gastric cancer has been reported¹³.

It can be assumed that patients with tumour positive nodes or local infiltration have had an incomplete excision (residual tumour). This view is supported by the fact that only 50 per cent of our patients who survived 30 days or longer were classified as stage I/II with a median survival of 16 months, compared with 7.5 months in the stage III group. From this experience, it is clear that 'curative' liver transplantation for primary hepatic malignancy can only be considered when the tumour is confined to the liver (stage I and II). Nevertheless, even in node negative cases, recurrence of tumour may occur, suggesting that micrometastatic seedlings were present at the time of transplantation.

Recently, the Pittsburgh team has embarked on a more radical approach, the so called 'cluster' procedure¹⁴. This involves *en-bloc* resection of the native liver, pancreas, duodenum, spleen, stomach, proximal jejunum and ascending and transverse colon and replacement by a composite 'cluster' consisting of liver, pancreas and duodenum removed *en-bloc* from the donor. Nine of 11 patients are alive at 1 to 6 months although the follow-up is insufficient to comment on recurrence of tumour. This procedure may reduce the incidence of residual

disease and local recurrence but long-term survival data is awaited.

In this series hepatocellular carcinoma with cirrhosis carries a poor prognosis. Only one patient survived for 12 months and, despite a complete resection, he subsequently died with bone metastases. The management of a patient with cirrhosis and a small tumour is controversial. Kinami *et al.*¹⁵ have shown a consistent correlation between tumour size in cirrhotic patients and time of recurrence after limited hepatic resection. Good results have also been obtained by the Pittsburgh group¹⁶ in patients who were transplanted for chronic liver disease and found at postoperative histology to have an incidental tumour (<5 cm); 13 of 14 patients are alive at follow-up of 3 to 73 months, six surviving beyond 3 years. The availability of intraoperative ultrasound scan^{17,18} has increased the number of limited segmental resections in patients with a small tumour and cirrhosis. The choice of partial excision *versus* liver replacement should be taken in the light of age, functional hepatic reserve, dysplasia¹⁹, portal hypertension and outcome.

The proportion of patients transplanted for the fibrolamellar tumour in this series is greater than in previous reports^{5,16,20}. In this series patients with fibrolamellar hepatocellular carcinoma presented late (four of six patients in stage III). Even with incomplete resection confirmed histologically, good palliation has been achieved in three patients with metastatic disease with a mean disease free interval of 14 months, one still alive at 34 months. When comparing the fibrolamellar variant with non-fibrolamellar hepatocellular carcinoma without cirrhosis, there appear to be similarities in the clinical outcome although our numbers are small. The macroscopic features and growth characteristics of the fibrolamellar hepatocellular carcinoma make it amenable to surgical excision. Ideally, patients with this type of tumour should be referred to a centre where the techniques of extended liver resection and OLT are available.

Cholangiocellular carcinoma in our experience has a bad prognosis (all three patients died with recurrence within 12 months of transplant). All our patients were stage III, and the Hannover group have reported similarly disappointing results for stage II tumour⁵.

Tumours of mesenchymal origin represent a spectrum of relatively benign to aggressive malignancy. Epithelioid haemangiomaendothelioma has been reported to have a relative benign course^{21,22}. This cannot be supported in our series as one patient presented with widespread metastases and another (3-years-old, OLT 241, infantile variant) in whom the massive tumour was growing at an alarming rate.

It is difficult to be accurate in tumour staging with nodal status during preoperative and intraoperative evaluation. Liver transplantation in our hands and others⁵ can clearly do little to help those in stage III disease with extended nodal involvement. While more radical surgical options are currently being explored, for the most part liver transplantation will be reserved for those patients with stage I and II without nodes who can expect a survival greater than 50 per cent at 2 years.

Routine staged histological assessment of porta hepatis and hepatic artery nodes should be performed at the time of hepatectomy before proceeding to grafting. The increased liver storage times now available²³, can permit liver grafting as a semi-elective procedure during 'working' hours when histopathological evaluation is more readily available. For the stage III patients, either a more radical surgical approach is needed, as is currently being explored, or a more effective combined chemotherapy schedule must be developed. In the meantime, the role of liver transplantation for hepatic malignancy will be limited.

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References

1. Iwatsuki S, Starzl TE. Personal experience with 411 hepatic resection. *Ann Surg* 1988; **208**: 421-32.
2. Starzl TE, Iwatsuki S, Van Thiel DH *et al*. Evolution of liver transplantation. *Hepatology* 1982; **2**: 614-36.
3. Pichlmayr R. Is there a place for liver grafting for malignancy? *Transplant Proc* 1988; **XX**: 487-82.
4. Kirby RM, McMaster P, Clements D *et al*. Orthotopic liver transplantation: postoperative complications and their management. *Br J Surg* 1987; **74**: 3-11.
5. Ringe B, Wittekind C, Bechstein WO, Bunzehl H, Pichlmayr R. The role of liver transplantation in hepatobiliary malignancy. *Ann Surg* 1989; **209**: 78-89.
6. Koneru B, Cassavilla A, Bourmen J, Iwatsuki S, Starzl TE. Liver transplantation for malignant tumours. *Gastroenterol Clin North Am* 1988; **17**: 177-93.
7. Shaw BW Jr, Martin DJ, Marguez JM *et al*. Venous bypass in clinical liver transplantation. *Ann Surg* 1984; **200**: 524-34.
8. Fortner JG, Maclean BJ, Kim DK *et al*. The seventies evolution in liver surgery for cancer. *Cancer* 1981; **47**: 2162-6.
9. *European Liver Transplant Registry*; H. Bismuth, Hôpital Paul Brousse, Villejuif, France, December 1988.
10. Angrisani L, Jurewicz WA, Clements DG *et al*. Liver transplantation for liver cancer. *Transplant Proc* 1986; **XVIII**: 1218-19.
11. Mittal R, Kowal C, Starzl TE *et al*. Accuracy of computerised tomography in determining hepatic tumor size in patients receiving liver transplantation or resection. *J Clin Oncol* 1984; **2**: 637-42.
12. Snow JH, Goldstein HM, Wallace G. Comparison of scintigraphy, sonography and computed tomography in the evaluation of hepatic neoplasm. *AJR* 1979; **2**: 915-18.
13. Park KGM, Chung SC, McGuire L, Li AK, Crofts TJ. Intra-operative assessment of lymph node involvement in gastric cancer. *Ann R Coll Surg Engl* 1989; **71**: 324-5.
14. Starzl TE, Todo S, Tzakis A *et al*. Abdominal organ cluster transplantation for the treatment of upper abdominal malignancies. *Ann Surg* 1989; **210**: 374-86.
15. Kinami Y, Takasshima S and Miyazaki I. Hepatic resection for hepatocellular carcinoma associated with liver cirrhosis. *World J Surg* 1986; **10**: 294-301.
16. Iwatsuki S, Gordon RD, Shaw BW Jr, Starzl TE. Role of liver transplantation in cancer therapy. *Ann Surg* 1985; **202**: 401-7.
17. Makuuchi M, Hasegawa H, Yamazaki S, Takayasu K, Moriyama N. The use of operative ultrasound as an aid to liver resection in patients with hepatocellular carcinoma. *World J Surg* 1987; **11**: 615-21.
18. Bismuth H, Castaing D, Garden OJ. The use of operative ultrasound in surgery of primary liver. *World J Surg* 1987; **11**: 610-4.
19. Ohnishi K, Tanabe Y, Ryu M *et al*. Prognosis of hepatocellular carcinoma smaller than 5 cm in relation to treatment: study of 100 patients. *Hepatology* 1987; **7**: 1285-90.
20. O'Grady JG, Polson RJ, Rolles K, Calne RY, Williams R. Liver transplantation for malignant disease: results in 93 consecutive cases. *Ann Surg* 1988; **4**: 373-9.
21. Ishak KG, Sesterhenn IA, Goodman MD, Rabin L, Stromeyer FW. Epithelioid hemangioendothelioma of the liver: a clinicopathologic and follow-up study of 32 cases. *Hum Pathol* 1984; **15**: 839-52.
22. Marino IR, Todo S, Tzakis AG *et al*. Treatment of hepatic epithelioid hemangioendothelioma with liver transplantation. *Cancer* 1988; **62**: 2079-84.
23. Jamieson NV, Sundberg R, Lindell S *et al*. The 24- to 48-hour preservation of canine liver by simple cold storage using UW lactobionate solution. *Transplant Proc* 1989; **21**: 1292-3.

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Case report

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Management of intrahepatic calculi in Caroli's disease by extracorporeal shock wave lithotripsy

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Caroli's disease was first described in 1958¹ and is a rare condition frequently complicated by stones of the intrahepatic ducts which can cause repeated episodes of acute cholangitis and liver abscesses. Sauerbruch and colleagues² showed that extracorporeal shock wave lithotripsy (ESWL) safely fragments stones in the gallbladder and the common bile duct. We report disintegration of large intrahepatic bile duct stones by ESWL in a patient suffering from Caroli's disease.

Case report

A 27-year-old Portuguese woman was admitted in 1984 for acute cholangitis. She had a history of gallstones which had been treated by

cholecystectomy 5 years previously. On admission, biochemical analysis showed a rise of the serum levels of alkaline phosphatase (1300 units/l), γ -glutamyltranspeptidase (850 units/l), aminotransferases (serum glutamic oxaloacetic transaminase, SGOT, 190 units/l and serum glutamic pyruvic transaminase, SGPT, 307 units/l), and total bilirubin (109 μ mol/l). Fever (39.0°C) and leucocytosis (white blood cell count 14000) were present. Blood cultures grew *Streptococcus fecalis* and *Haemophilus influenzae*. Ultrasound showed several dilated intrahepatic bile ducts containing echogenic material, mostly in the left hepatic lobe. Endoscopic retrograde cholangiography confirmed the presence of stones in the intrahepatic bile ducts. With medical treatment the condition of the patient improved and a left lobectomy was considered. At laparotomy the left hepatic lobe was found to be firm and irregular with marked fibrous changes. Stones were found in the right lobe of the liver and removed from segments 1 and 8 using a balloon catheter and choledochoscopy through a choledochotomy. The common bile duct was drained via a T tube. The postoperative course was uneventful. A cholangiogram was performed on the tenth postoperative day and residual stones were found in segment 1. The dissolution of the stones using CAPMUL (Pharmacie des Hôpitaux de Paris) by continuous perfusion via the T tube was attempted, but had to be stopped after 48 h because of biliary pain and vomiting. Liver function tests returned to normal and the patient was discharged in August 1984 after removal of the T tube.

The patient had no complaint for 21 months. Further episodes of acute cholangitis occurred in June 1986. Ultrasonography and endoscopic retrograde cholangiography showed stones in segments 1 and 7. Reoperation was performed for biliary decompression. Stones near the choledochotomy were removed but it was impossible to clear the biliary tree. Postoperative cholangiography showed some small residual stones and dissolution by oral chenodeoxycholic acid (15 mg/kg of body-weight per day) was attempted. The patient left hospital at the end of June 1986. She was readmitted in October 1987 for an episode of acute cholangitis. Radiological examination showed two large calculi (30 mm and 25 mm) in segment 1 (Figure 1). Extracorporeal lithotripsy, using a piezoelectric lithotripter (FDAP LT01, EDAP International S.A., Marne-la-Vallée, France)³ with ultrasonographic detection, was performed with the patient lying in