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Repeated resection for malignant liver tumours

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Fifteen repeat hepatic resections were performed on 12 patients with either recurrent or residual malignant tumours of the liver. Of these, one patient underwent three repeat resections and another underwent two. Five had primary liver tumours and seven had liver metastases. Planned, 'staged', repeat resections were performed on three patients because of multiple deposits of tumour, cirrhosis or extensive disease at initial presentation. There was no operative mortality. The period of follow-up from the time of repeat resection ranged between 4 months and 36 months during which two patients died from recurrent disease. The mean survival after the repeat resection was 16.8 months (range 4–36 months). Although technically demanding, repeat hepatectomy is feasible and may provide similar benefits.

Untreated, primary and metastatic tumours of the liver relentlessly and universally progress to the death of the patient. This is the main incentive for surgeons to attempt aggressive liver resection, aiming for cure in early cases and palliation in late cases. The ability of the normal liver to regenerate *(1)* encouraged surgeons to repeat resection for further recurrence, or to stage resection for multiple or large tumours *(2–7)*. We report our experience in 12 cases of 15 repeated liver resections.

Patients and methods

Between October 1989 and February 1993, 15 repeat hepatectomies were performed on 12 patients with hepatic malignancies in the HPB Unit of the Hammersmith Hospital. One patient underwent three repeat resections and one underwent two repeat resections. All operations were performed by one surgeon (NH). The technique used has been described in a previous publication *(8)*. Total vascular exclusion (TVE) was used in eight repeat resections and inflow occlusion (Pringle manoeuvre) in seven. All except two patients had their first liver resection at the Hammersmith Hospital. Pathological data are presented in Table I. Anatomical segments referred to are those described by Couinaud *(9)*. After liver resections for malignant tumours, all patients are referred to the oncology unit for advice regarding adjuvant therapy. It has been our policy to administer 5-fluorouracil (5FU) and folinic acid to patients with secondary liver tumours in whom the resection was not complete or in the presence of extrahepatic metastases. Postoperatively, patients with cholangiocarcinoma received 5FU, folinic acid and radiotherapy, while those with hepatocellular carcinoma were administered α-interferon and 5FU. Repeat resections consisted of resection of three segments in one repeat procedure, two segments in another, one segment in six was excised and seven non-anatomical resections (NAR).

Metastatic colorectal carcinoma (MCRC) was the most common pathology (five patients with eight resections), followed by hepatocellular carcinoma (HCC, four patients) and metastatic breast cancer, metastatic small intestinal stromal tumour, and cholangiocarcinoma (one each). Of the patients with colorectal cancer, one underwent three repeat resections and another underwent two repeat resections (Table II).

In all cases of metastatic liver disease, no extrahepatic metastases were detected at the time of primary tumour resection, except one patient who had peritoneal deposits of breast carcinoma.

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Table I. Patients and tumour characteristics in 12 patients undergoing repeat liver resection

No	*Age/sex*	*Type of tumour*	*Gross picture of initial tumour*	*Resection margin after first resection*	*Recurrence after first resection*	*Detection of initial recurrence*
1	47/F	Metastatic CRC	Solitary	Free	Solitary	CT
2	53/F	Metastatic CRC	Multiple	Free	Multiple	CT
3	46/F	Metastatic CRC	Solitary	Free	Solitary	CT
4	58/F	Metastatic CRC	Solitary	Free	Solitary	CT
5	65/F	Metastatic CRC	Solitary	Free	Solitary	CT
6	51/F	Metastatic breast cancer	Solitary	Free	Multiple	CT
7	70/M	Metastatic small bowel stroma cell tumour	Multiple	Staged repeat	Staged repeat	Staged repeat
8	55/M	HCC	Multiple	Staged repeat	Solitary staged repeat	Staged repeat
9	59/F	HCC	Multiple	Staged repeat*	Staged repeat	Staged repeat
10	25/F	HCC	Solitary	Free	Solitary	CT
11	76/M	HCC	Solitary	Free	Solitary	CT
12	57/M	Hilar cholangio-carcinoma	Solitary	Not free	Solitary	Jaundice

NB: The histopathological finding of the recurrence was the same as first tumour
* Cirrhotic patient

Table II. Repeat liver resection and survival

No	*1st Hepatectomy*	*Interval (months)*	*Repeat*	*Survival*	*Chemo-therapy*
1	Right hepatectomy	6	1st Repeat: segmentectomy IV and I	19 months from 1st repeat and 6 months from last repeat†	
		6	2nd Repeat: NAR from left lobe		+
		7	3rd Repeat: NAR from left lobe		
2	Segment V and part of segment IV	12	1st Repeat: NAR from segments IV+VIII	22 months from 1st repeat and 7m from last repeat*[1]	
		15	2nd Repeat: excision segment VII		+
3	V and VI segment	7	Excision of segment IV b	19 months*[1]	–
4	Segment II and III	6	Segment IV	7 months*[1]	–
5	Segment V and VI	7	NAR from segment IV	7 months†[2]	+
6	Left hepatectomy	108	NAR of four nodules from the right lobe + R/O peritoneal deposits	23 months*[1,3]	+
7	Right hepatectomy + NAR of nodule in segment II and injection of absolute alcohol in nodule in segment III	3	Segment III	4 months*[1]	–
8	Left hepatectomy + injection of absolute alcohol in a nodule in segment VII	12	Segment VII	11 months*[2,4]	+
9	Left hepatectomy	3	NAR of three nodules from segments V, VII and VIII	10 months*[2]	–
10	Right hepatectomy	54	NAR of tumour in segment II, III and IV	47 months*[1]	–
11	Left lobectomy	18	Segment IV	36 months*[2]	–
12	Localised excision of the tumour with hepaticojejunostomy	12	Right hepatectomy	14 months*[2]	–

* Living
† Died
[1] No recurrence in the liver
[2] Recurrence in the liver
[3] Pelvic metastasis well controlled by chemotherapy
[4] Underwent another laparotomy at 5 months but found unresectable

The first hepatic resection was major (three segments or more) in six patients, two segments in four patients and one segment in the remaining two. The resection margin was histologically free of tumour after the first liver resection in eight patients. In three patients the repeat resection was planned (ie it was a staged resection, the tumour was knowingly left behind, either at the resection margin or as separate deposits). The liver was cirrhotic in one (no. 9) and the tumours were multiple in the other two (no. 7 and 8). In those patients with residual tumour, absolute alcohol was injected with the hope of preventing progression of the disease until further surgery could be performed. One patient (no. 12) had undergone a palliative hilar resection for cholangiocarcinoma and presented subsequently with cholangitis. Re-evaluation showed that a further resection was possible to clear the tumour. The resection margin was close but macroscopically clear and he was treated with postoperative radiotherapy. Recurrence was detected at follow-up CT scan in those who had complete clearance at the first hepatic resection. The mean interval between resections was 16.4 months (range 3–108 months).

Results

There were no 30-day operative mortality or postoperative hospital deaths. There was one major intraoperative complication due to inferior vena cava (IVC) tear. This occurred in a patient undergoing the third repeat liver resection because of tumour recurrence. The IVC tear was in the suprahepatic IVC and extended up towards the diaphragm. This was repaired with a pericardial patch after thoracotomy. This necessitated total vascular arrest and cardioplegia after total body cooling down to 18°C. This patient recovered well and was discharged 2 weeks after operation. Postoperatively, there were transient biliary leaks in three patients with volumes less than 500 ml daily and all three stopped spontaneously within 1 month. One patient developed pleural effusion and was treated successfully with percutaneous aspiration.

Five patients remain disease free; follow-up being 4–36 months (mean 20 months) from the time of last resection. The mean survival of all patients from first repeat resection is 16.8 months (range 4–36 months). One patient has no further liver recurrence but has a pelvic tumour recurrence. Two patients have died from tumour recurrence with liver metastases; the first after 19 months and the other after 7 months from the time of the first repeat resection. Of the four patients with HCC, only one patient remains disease free at 47 months, the others are still alive but developed tumour recurrence (range 10–36 months; mean 21.75 months).

Discussion

Techniques for liver resection have progressed such that many primary and metastatic liver tumours, previously deemed inoperable, can now be safely resected. The phenomenon of liver regeneration after resection allows surgeons to repeat resection and even to plan for it (*2–7*) (Table III). This report analyses 15 repeat liver resections in 12 patients with primary and metastatic liver tumours. There was no operative mortality. In this series, the period of follow-up ranged between 4 months and 47 months (mean 16.8 months). Death from tumour recurrence occurred in two patients during this short period of follow-up.

Tumour recurrence in the liver after complete excision at the final repeat procedure has occurred in 50% (6/12) of times with a follow-up of 4 months to 36 months. Longer follow-up is needed to assess critically whether repeat resection is worthwhile. It is important to consider whether the benefits outweigh the risks in such patients. Justification of this procedure can only be addressed by a controlled prospective trial comparing the benefits in survival and quality of life between conservative treatment and aggressive surgery. Any potential benefits should be weighed against postoperative morbidity and mortality.

Three patients demonstrated the new concept of staged resection. In this situation subtotal tumour excision is performed with the intention of further resection when the liver has regenerated. The first hepatic resection was an extended right hepatectomy with a non-anatomical resection of a nodule in segment three and alcohol injection into another nodule in segment three. Wider resection of these two nodules was not possible because of the size of the remaining liver. Three months later, after regeneration, segment three was excised. He remains disease free at 6 months after the second procedure. The second patient had multifocal hepatocellular carcinoma and underwent an extended left hepatectomy of the bulk of the tumour at the first operation. Further resection of segment VII was performed after regeneration. Both patients had alcohol injected into their residual tumour at the first operation with the hope of halting progression of disease during regeneration. These two patients are alive and well 11 months and 10 months, respectively, after repeat resection. The third procedure was performed on a cirrhotic patient (Child's A). She underwent a left hepatectomy as the first stage and then multiple NAR at the second stage. Resection of all lesions in one operation would have been very risky as it could have induced postoperative liver insufficiency. In this two-stage approach we always radically resected the tumour on one side and waited for regeneration and then radically resected the residual tumour at the contralateral side. At no time have we cut across tumour tissue at the first stage of the procedure.

It has been our policy not to consider for repeat resection patients with extrahepatic disease, cancer cachexia or jaundice owing to tumour replacement of liver parenchyma, as these patients universally have a very poor prognosis. Technically, repeat resection is more demanding as all the dissection planes have already been disturbed. Mobilisation of the hilar structures and inferior

Table III. Reported series of repeated hepatic resection for malignant liver tumours

Author	*Type of tumour*	*First HR*	*Interval (months)*	*Second HR*	*Survival (months)*			*Reported morbidity and complications*
					AFD	*AWD*	*Dead*	
Nagasue *et al (2)*	HCC	1 Mj	4–28	1 Mn	4/9	2/9	3/9	2/9
9 patients		1 Mn		1 S	3–37	11 and 20	4–17	Biliary fistula and subhepatic abscess
9 repeats		3 S		7 NAR				
		4 NAR						
Nordlinger *et al. (3)*	MCRC	2 Mn	5–40	5 Mj	2/6	3/6	1/6	Not reported
6 patients		4 NAR		1 Mn	2 and 12	14–28	10	
6 repeats								
Lange *et al. (4)*	11HCC	19 Mj	3–132	6 Mj	8/28	5/28	14/28	15%
28 patients	9 MCRC	2 Mn		6 Mn 12S	1–54	6–47	6–52	
34 repeats	8 Misc.	1 S		7 NAR				
		6 NAR		1 Mj†			1*	
				4 NAR†				
				1 T†				
Huguet *et al. (5)*	9 HCC	9 Mj	4–40	7 Mj	6/19	4/19	6/19	12/21 Only 2 needed operative
19 patients	8 MCRC	1 Mn		2 Mn	18–56	20–51	3–89	intervention
21 repeats	2 Misc.	9 NAR		3 S			2* after	1 POD
				7 NAR			32 and 36	
				1 NAR†				
				1 T				
Griffith *et al. (6)*	MCRC	1 Mj	1–39	6 Mj	7/9	1/9		1 POD
9 patients		8 NAR		3 NAR	9–67	16		
9 repeats								
Valliant *et al. (7)*	MCRC	16 Mn	6–40	10 Mj	4/16	3/16	6/16	6/18 Reversible complications,
16 patients				3 Mn	26–93	8–10	14–61	1 died 2 weeks after transplantation
18 repeats				2 NAR				
				1 Mn†				
				1 NAR†				
				1 T				

HR, Hepatic resection
HCC, Hepatocellular carcinoma
MCRC, Metastatic colorectal carcinoma
Misc, Miscellaneous metastatic cancer
Mj, Major hepatic resection
Mn, Minor hepatic resection
S, Segmentectomy
NAR, Non-anatomical resection
* Lost to follow-up
† Second repeat HR
‡ Third repeat HR
T, transplantation
POD, Postoperative death

vena cava can be particularly challenging. In our experience second repeat resections are more difficult than first repeat resections.

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