CLINICAL RESEARCH

Prediction of early death after therapeutic hepatic arterial embolisation

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Abstract

A consecutive series of 14 patients with hepatic malignant disease treated by palliative hepatic arterial embolisation was reviewed. Twelve patients had hepatic pain from their tumour and two were suffering from the carcinoid syndrome. Six patients died within four weeks of the procedure (group 1) and eight survived for at least 10 weeks (group 2). Factors were sought that might permit prediction of a high risk of early death (group 1). The pre-embolisation angiograms reviewed by a "blind" observer showed no differences in vascularity or tumour size between the groups and no difference in the extent of arterial occlusion after embolisation. The portal vein was patent in all patients. No significant difference was seen between the groups in the pre-embolisation biochemical values, with the exception of lower serum albumin concentrations and higher alkaline phosphatase activities in group 1. All those who died early had serum alkaline phosphatase activities of 45 KAU or above, while six of the eight who survived longer had activities below this value ($p < 0.02$).

These findings suggest that serum alkaline phosphatase activity of 45 KAU or more (normal range 3-13) might alone be a useful predictor of early death. Stepwise discriminant analysis using a weighted combination of serum alkaline phosphatase activity and albumin concentration predicted the outcome in all but one of the patients studied ($p < 0.002$).

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Introduction

Hepatic arterial embolisation was used as palliative treatment in 14 patients with primary or secondary tumours of the liver; 12 had severe pain and two the carcinoid syndrome. Six patients died within 28 days after embolisation, and at least four of these deaths were attributed to the procedure. Because of this high mortality we abandoned the procedure, but follow up showed that the other eight patients obtained useful palliation and survived for up to 14 months. Radiological and laboratory data obtained before embolisation were therefore analysed in order to see if they might be used to predict a high risk of early death and to permit future use of the treatment in selected patients likely to benefit.

Methods

The case notes and angiograms of 14 consecutive patients with extensive hepatic tumours treated between January 1978 and May 1981 were examined and data obtained just before embolisation extracted (see table II). The extent of malignant disease within the liver was estimated from the pre-embolisation arteriograms by tracing the outlines of the areas of pathological circulation and expressing them as a percentage of the total area of the liver. Each patient underwent a single hepatic arterial embolisation with combinations of absorbable gelatin sponge (Sterispon), homologous lyophilised dura mater (Lyodura), and human thrombin under antibiotic cover. The aim was completely to occlude the arterial supply to the tumour, and the extent of the occlusion was assessed angiographically immediately after embolisation. The portal vein was patent in all patients.

Results

Figure 1 shows a life table plot of the survival of the patients. Six died within 28 days of the procedure (group 1), but eight (group 2) lived at least 70 days, the longest documented survival being 14 months. The primary conditions in group 1 were one case of pancreatic carcinoid and five cases of carcinoma (one colorectal, three pancreatic, and one hepatocellular). In group 2 one patient had carcinoid and seven had carcinomas (two colorectal, two gastric, one prostatic, and two hepatocellular).

All three hepatocellular tumours occurred in the presence of established hepatic cirrhosis. All 14 patients had vascular tumours

TABLE I—*Details of patients who died within 28 days of procedure (group 1)*

Case No	Sex	Age (years)	Chemotherapy	Day died	Cause of death
1	M	60	Yes	2	Carcinoma pancreas, bronchopneumonia
2	M	54	No	4	Carcinoma pancreas, carcinomatosis
3	M	75	Yes	4	Hepatoma, hepatitis B surface antigen + cirrhosis, hepatorenal failure
4	M	65	No	8	Pancreatic carcinoid (embolised), liver abscess, peritonitis
5	F	77	No	22	Carcinoma rectum, extensive metastases, inferior vena caval obstruction (no necropsy)
6	M	52	Yes (after procedure)	25	Pancreatic carcinoma. Died at home (no necropsy)

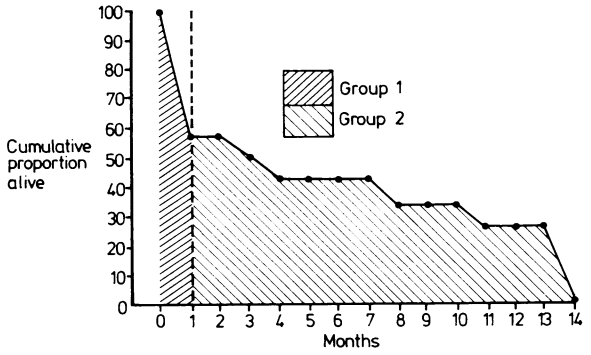

FIG 1—Cumulative proportion of patients remaining alive up to 14 months after embolisation procedure. Group 1 died by definition within 28 days; group 2 lived longer.

(graded 1 or 2 on a 0-3 scale).[1] In group 1 there were five men and one woman with a mean age of 64 years (range 52-77). Group 2 comprised five men and three women with a mean age of 61 (28-77). Table I shows the causes of death of the six who died within 28 days of embolisation. This table also gives the timing of these early deaths together with age and sex and whether or not adjunctive chemotherapy was used. Table II compares the pre-embolisation data in the two groups. As shown angiographically, the mean area of the liver occupied by tumour circulation was 67·2% (range 46-90) in those who died early and 58·8% (range 28-92) in those surviving more than 28 days (NS). Similarly, the mean estimated proportion of the hepatic arterial supply occluded during embolisation was 88% (range 70-100) in group 1 and 71% (range 20-100) in group 2 (NS). Serum albumin concentrations were lower in group 1 (mean 29·3 (SEM 1·2) g/l) than in group 2 (mean 33·8 (SEM 1·3) g/l) and alkaline phosphatase activities higher in group 1 (mean 112·5 (SEM 33·1) KAU) than in group 2 (mean 42·6 (SEM 8·9 KAU). All those who died within 28 days had alkaline phosphatase activities of 45 KAU or above, while six of the eight surviving longer had activities below 45 KAU ($p<0·02$).

Stepwise discriminant analysis showed that a function (F) derived from $F = -8·222 + 0·297$ plasma albumin (g/l) $-0·020$ serum alkaline phosphatase (KAU; normal range 3-13) predicted the outcome in all but one of the patients ($p<0·002$). F was less than $-0·2$ in group 1 patients. Significance testing of F in each patient showed that seven of the 14 patients could be assigned to their group with an insignificant ($p<0·05$) chance of incorrect placing (fig 2).

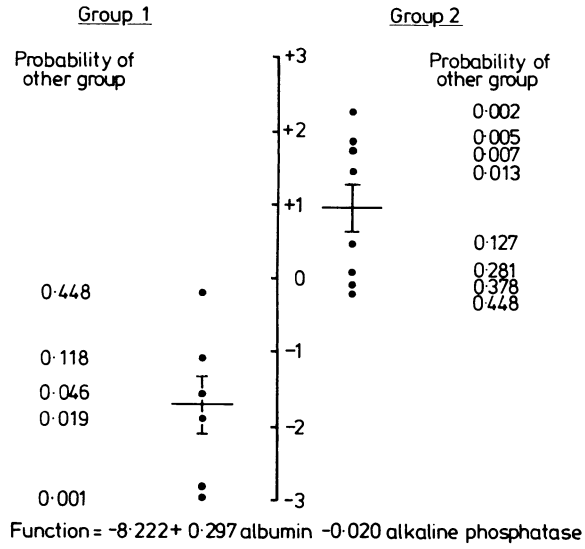

FIG 2—Values for function F (bars represent SEM) calculated from weighted combination of serum albumin concentration (g/l) and alkaline phosphatase activity (KAU). Calculated probability of F incorrectly predicting outcome (group) is given for each patient.

TABLE II—*Comparison of pre-embolisation data in groups 1 and 2 defined by outcome (rank sum or unpaired t test)*

	Group 1 (died within 28 days)	Group 2 (lived >70 days)	p
Tumour "volume" (rank)			NS
Tumour vascularity (0-2)	1·00	1·25	NS
Bilirubin (μmol/l)	35·7	38·9	NS
Total protein (g/l)	64·2	71·9	NS
Urea (mmol/l)	5·4	5·2	NS
Sodium (mmol/l)	131·0	135·0	NS
Potassium (mmol/l)	4·4	4·1	NS
Haemoglobin (g/dl)	11·9	11·0	NS
Prothrombin ratio	1·2	1·1	NS
Albumin (g/l)	29·3	33·8	<0·04
Alkaline phosphatase (KAU)	112·5	42·6	<0·04

NS = Not significant.
Conversion: SI to traditional units—Bilirubin: 1 μmol/l ≈ 0·06 mg/100 ml. Urea: 1 mmol/l ≈ 6 mg/100 ml. Sodium: 1 mmol/l = 1 mEq/l. Potassium: 1 mmol/l = 1 mEq/l.

Discussion

The death rate in our series, which comprised patients with extensive tumours treated principally for palliation of pain, contrasts with the low or absent mortality in larger series,[2 3] where limited embolisation was usually used on several occasions to achieve piecemeal arterial occlusion and total embolisation of the hepatic artery was reserved for patients with limited liver metastases and well preserved liver parenchyma. For palliation we chose to carry out a single embolisation procedure rather than expose the patient to repeated hospital admissions, angiography, and postembolisation pain and fever.

Our study suggests that the serum alkaline phosphatase activity and albumin concentration may be used to select those patients with symptoms who might benefit from our approach. The difference in albumin concentration still remained significant when the three patients with cirrhosis were excluded.

Other studies have suggested several adverse prognostic factors. It is generally agreed that those with the largest tumours are most at risk; however, if the technique is to be used for palliation of pain then large tumours will need to be treated. We found no significant difference in tumour load as assessed angiographically between those who died early and those surviving longer, and a very much larger series would be needed to see if the trend for larger tumours to fall into group 1 proved real. The technique used to assess tumour size probably overestimated the extent of disease, as it ignored the anteroposterior dimensions of the tumour masses. It did, however, provide a rough estimate of the extent of malignant disease. Neither alkaline phosphatase activity nor serum albumin concentration showed any tendency at all to correlate with tumour size.

Kim and colleagues suggested that the tumours that look most vascular after hepatic arterial angiography respond best to arterial embolisation.[1] This presumably indicates a greater dependence of these tumours on the arterial rather than portal blood supply. We found a similar though statistically non-significant trend.

Experiments in animals show that embolisation of the hepatic artery with relatively large particles of absorbable gelatin sponge results in less derangement of liver function and less risk of hepatic failure or abscess than embolisation of the more peripheral hepatic tree with silicone cement.[4] Embolisation of small vessels, however, is more effective in delaying the formation of a collateral circulation. Our technique used combinations of absorbable gelatin sponge, human thrombin, and Lyodura. Absorbable gelatin sponge and strips of Lyodura approximately 1×10 mm were used as the initial embolising materials, and human thrombin was added when satisfactory occlusion had not been achieved. Thus our technique may have resulted in relatively proximal arterial occlusion and spared the terminal arteries and arterioles.

Portal venous obstruction is an absolute contraindication to hepatic arterial embolisation and hepatic cirrhosis a relative contraindication; in cirrhosis the liver parenchyma is more dependent on the hepatic arterial supply than normal. Nevertheless, two of the three patients we treated who had cirrhosis survived longer than 28 days; one woman aged 47 died at 11 months, and another woman aged 28 was still alive at three months when she returned to her own country and was lost to follow up.

Jaundice has also been suggested as a relative contraindication to hepatic dearterialisation,[5] though this has been disputed.[6] Only five of our patients had serum bilirubin concentrations within the normal range (two in group 1, three in group 2), and we did not find the serum bilirubin concentration useful in predicting outcome in this high risk group of patients. Tumours may produce localised intrahepatic biliary obstruction,[7] and embolisation experiments in monkeys[8] show an increased risk of abscess formation in areas of liver whose biliary outflow is obstructed. Local biliary obstruction may explain the predictive value of the raised serum alkaline phosphatase activity. The preponderance of pancreatic tumours in group 1 is noteworthy.

Our findings suggest that a weighted combination of serum alkaline phosphatase activity and serum albumin concentration may be used to predict a subgroup of patients with extensive hepatic tumours who can be treated with hepatic arterial embolisation. Our findings could be readily tested in other series retrospectively before clinical application and, if confirmed, would permit safe single palliative embolisation of large painful tumours.

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Resolution after radiotherapy of severe pulmonary damage due to paraquat poisoning

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Abstract

A 29 year old man was admitted 36 hours after ingesting about 5 g paraquat. His arterial oxygen pressure fell progressively to 3·4 kPa (34 mm Hg), and pulmonary damage induced by paraquat was diagnosed. His condition did not improve after treatment with prednisolone and cyclophosphamide, but after irradiation both lungs cleared and arterial oxygen pressure started to improve. Irradiation of the lungs should be considered in patients who, after surviving the acute phase of poisoning with paraquat, show progressive deterioration of respiratory function.

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Introduction

Pulmonary disease induced by paraquat has an almost uniformly fatal outcome. We describe a patient in whom the pressure of arterial oxygen fell to 4·6 kPa (34 mm Hg) despite treatment with a combination of cyclophosphamide and prednisolone but whose condition improved after radiotherapy to the lungs.

Case report

A 29 year old man was admitted to hospital because he said that he had taken some Weedol a few hours earlier. Urine screening by the alkaline dithionate method confirmed the presence of paraquat. After undergoing stomach washout he was treated with fuller's earth. Charcoal haemoperfusion was started but was stopped when the serum paraquat concentration on admission was found to have been only 429 μmol/l (80 mg/l). He later admitted that he had taken two packets of Weedol (5 g paraquat) 36 hours before coming to hospital.