costs. This analysis will need to take account of the potential to move care from the inpatient ward to the day-case unit as we have done. It is only when this and other similar comparisons have been made that we will be able objectively to compare the cost benefit outcomes of the different regimens.

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Possible Prognostic Significance of P53 Immunoreactive Status of Hepatic Colorectal Cancer Metastases Following Surgical Resection

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THE EXPRESSION of the mutant p53 protein has been demonstrated to have poor prognosis significance following surgical resection of colorectal adenocarcinoma [1]. These data have been recently confirmed by immunohistochemical analysis of the p53 antigen in paraffin slides [2]. The prognostic significance of *Tp*53 mutation in liver metastases from colorectal cancer has not been evaluated. We report here a retrospective study with the aim of assessing the possible relationship between p53 status of hepatic metastases from colorectal cancer and outcome following hepatectomy.

102 patients who underwent liver resection for colorectal metastases in our unit from 1983 to 1989 (at least a 6-year follow-up) were reviewed. We excluded all patients for whom liver resection had not been curative and/or patients who had received pre-operative chemotherapy. Pre-operative chemotherapy was considered to change the immunohistochemical results due to necrosis of the tumour.

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Table 1. *Nuclear overexpression of p53 in colorectal hepatic metastases according to the clinical outcome*

	p53+++	p53++	p53+	p53+/+++	p53−
DFS ($n=10$)	3 (30%)	1 (10%)	0 (0%)	4 (40%)	6 (60%)*
HR ($n=11$)	2 (18%)	3 (27%)	4 (36%)	9 (82%)	2 (18%)

DFS, disease-free; HR, hepatic recurrence; +++, nuclear staining above 60%; ++, 30–60%; +, 5–30%; −, absence of nuclear staining or below 5%. *$P=0.08$ (Fisher's exact test).

As a preliminary approach, two groups of patients with opposite outcomes following liver resection were evaluated. One group consisted of 10 patients alive and disease-free for more than 4 years following resection (DFS group), whilst the second group consisted of 11 patients who demonstrated intrahepatic recurrence within 1 year from resection leading to death within 2 years from surgery (HR group).

An immunohistochemical evaluation was performed by a single pathologist unaware of the medical history and outcome of patients. Formalin-fixed paraffin-embedded sections of liver metastases were studied for expression of p53 protein using the antibody DAKO-p53, DO7.

Results were expressed in a semiquantitative manner (Table 1). Other prognostic factors such as age, sex, latency of liver metastases, pre-operative serum carcinoembryonic antigen (CEA), number and maximum size of metastases as well as margin of resection were correlated to ultimate patients' outcome following surgery.

Patients' survival was significantly different between the two groups (7.2 ± 1.9 years for the DFS group compared with 1.1 ± 0.6 years in the HR group). The maximum size of metastases was higher in the HR group than in the DFS group (59.7 ± 25.7 versus 36.0 ± 21.6 mm; $P=0.03$, test *t*). Serum levels of CEA were also increased in the HR group (112 ± 163 versus 11 ± 14 ng/ml) ($P=0.07$). The other factors were comparable between groups.

Positive immunohistochemical staining for p53 was more frequently observed in the HR group (82%) than in the DFS group (40%), but the difference was not significant ($P=0.08$). Sensitivity of p53 immunohistochemical expression for predicting early liver recurrence was 6/10 (60%) while specificity was 9/11 (82%). The positive predictive value was 6/8 (75%) while the negative predictive value was 9/13 (69%).

The small number of patients evaluated in these series does not allow a definitive conclusion that p53 wild-type status is an independent prognosis factor. However, the encouraging results observed provide a basis for further investigation as the p53 status determined by immunohistochemistry could be part of the decision-making process of adjuvant therapy following curative resection of colorectal liver metastases.

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