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DIFFERENTIAL EFFECTS OF TACROLIMUS (FK506) AND CYCLOSPORINE ON LIVER ALLOGRAFT HISTOPATHOLOGY.

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Background: A predominant shift from cyclosporine (CsA) based immunosuppressive regimens to tacrolimus (FK506) for orthotopic liver transplantation (OLT) took place at our institution in the mid-1990's. FK506 has been touted as decreasing acute rejection and steroid dependence as well as having a toxicity profile no worse than CsA. Differential effects of FK506 and CsA on hepatic histopathology have only been assessed over the short term in small studies with mixed results. Anecdotally, an increase in centrilobular necrosis was suspected in patients treated with FK506. Aim: To assess complication rates between FK506 and CsA by comparing histologic features using long-term protocol follow-up biopsies. Methods: 60 patients (pts)—30 each FK506 and CsA—were selected on the basis of OLT between 8/94-5/96. Exclusion criteria were limited to: use of opposing drug >1 week, <1 year histologic follow-up or a native diagnosis of autoimmune hepatitis. The two groups were very similar with regard to pretransplant diagnosis, mean age, and mean length of histologic follow-up (2.3 yrs FK506, 2.5 yrs CsA). All biopsies at ≥3 months post OLT were reviewed specifically for portal, periportal or lobular inflammation, bile duct status, ductular proliferation, cholestasis, steatosis, fibrosis, centrilobular necrosis, recurrent primary disease and rejection. Results: An increase in hepatocanalicular cholestasis was noted in the FK506 group at any time point (9/30 FK506; 2/30 CsA) and at time points ≥1 yr (7/30 FK506; 0.30 CsA). Of the cholestatic FK506 cases, one case demonstrated recurrent hepatitis C with fibrosis and 2 had biliary strictures. After exclusion of these cases, there was not a significant difference in cholestasis between the groups (p=0.12). A slight trend toward increased lobular inflammatory activity was seen in the FK506 group (12/30 FK506; 6/30 CsA, p>.05). No difference between the groups was found with portal/periportal hepatitis (14/30 each group), ductular proliferation (9/30 each group), steatosis (10/30 FK506; 9/30 CsA), fibrosis (3/30 FK506; 2/30 CsA), late rejection (1/30 each group), recurrent disease (5/30 FK506; 4/30 CsA) or centrilobular necrosis (8/30 FK506; 5/30 CsA). Conclusions: FK506 and CsA had similar rates of abnormal histologic parameters. While rates of cholestasis were increased in the FK506 group, this did not retain statistical significance when identifiable causes were eliminated. Of note, a significant difference in rates of centrilobular necrosis was absent.

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RADIOFREQUENCY (RF) ABLATION WITH COOLED NEEDLE ELECTRODE OF HEPATOCELLULAR CARCINOMA IN PATIENTS WITH COMPENSATED CIRRHOSIS.

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Background: Most patients with hepatocellular carcinoma (HCC) are not suitable for resection or transplantation due to size and location of the tumor, multifocality or inadequate functional hepatic reserve. Local application of termal energy produces dessication and necrosis of tumor cells. AimTo assess the efficacy of local RF-ablation with cooled needle electrode in 19 patients with compensated histologically proven cirrhosis and with unresectable HCC of less than 5cm in diameter. Patients and Methods: The tumor was detected by ultrasound examination of abdomen during prospective follow-up of patients at risk and was confirmed by ultrasound-guided fine needle biopsy. 19 cirrhotic patients (69yr, 15 men, 14 HCV+, 1 AFP> 200ng) were enrolled, 18 had a single node and 1 two nodes (63% tumor size < 3cm). Patients were treated under general anesthesia and ultrasound guidance using cooled needle electrode RF generator (Radionics RFG-3E) that was delivered for 12-36 minutes. Response to therapy was assessed by triphasic CT, serum alphafetoprotein (AFP, n.v. <7ng/ml) and survival. All patients were followed to assess complications, efficacy of treatment and recurrence of illness. Results: 42% of 19 patients received ablation therapy only, 47% RF-ablation + percutaneous ethanol injection and 11% RF-ablation + transcatheter arterial chemoembolization. 95% had partial response to therapy, no complications were founded and all patients are alive at 12 month of follow-up. ConclusionsRF ablation is safe, well-tolerated and relatively efficacious for treating less than 5cm unresectable HCCs. However, randomized studies are necessary to assess the cost efficacy of the procedure in comparison with percutaneous ethanol injection therapy.

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THE COURSE OF FOCAL NODULAR HYPERPLASIA (FNH) IN 24 ASYMPTOMATIC CARRIERS.

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Background: FNH is a benign lesion of the liver characterized by focal hyperplasia of hepatic parenchyma with a central scar of fibrosis around an abnormal artery. FNH is an asymptomatic mass that is often incidentally detected, that should be differentiated from hepatic adenoma and hepatocellular carcinoma. Aimwe describe the clinico-pathological features of 24 patients with symptomless FNH incidentally detected by abdominal ultrasound (US). Patients and Methods: 24 patients (M 5; F 19; M/F 1:4) were enrolled between June 1988 and November 1999 with a liver mass found during US examination for unrelated reasons. The commonest indications to US were abdominal discomfort and dispepsia. Fine needle biopsy (FNB) was carried out in all patients by Tru-Cut 21 Gauge with a diagnostical accuracy of 100% and no complications. 21 patients (87.5%) had a single node with a diameter ≤3cm in 23.8% of patients, 3-5cm in 42.9%, > 5cm in 33.3%. 3 patients (12.5%) were multifocal. Results: After 10yr of follow-up (126: 11-137 months) 100% patients were alive. In 3 patients (13%) lesions had increased in size without specific liver-related symptoms. Conclusions: FNH nodes are usually discovered incidentally during US examination performed in patients complaining aspecific gastrointestinal symptoms. A 10-yr follow-up showed that the disease is not progressive and that surgical therapy is usually not necessary.

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TRANSJUGULAR INTRAHEPATIC PORTA-SYSTEMIC SHUNT (TIPS) VS.ENDOSCOPIC SCLEROTHERAPY (ES) FOR THE PREVENTION OF VARICEAL REBLEEDING IN CIRRHOSIS: A META-ANALYSIS USING INDIVIDUAL DATA OF 432 PATIENTS FROM 5 RANDOMIZED CONTROLLED TRIALS.

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Background:Between 1996 and 1998, 6 randomized controlled trials comparing ES and TIPS for the prevention of rebleeding in cirrhotic patients have been published. Aim:to combine the individual patients data of the trials and to identify prognostic variables for major end-points.Methods: the Authors of 5 of the 6 trials agreed to provide individual patients data, including complete follow-up data.Analysis was carried out with the BMDP statistical package.The major end-points analyzed were rebleeding, death and encephalopathy. Kaplan-Meier plots of these end-points were compared by the log-rank test. Prognostic variables were identified by univariate analysis and by Cox's proportional hazard models. Results: The 5 trials included 432 patients:213 treated by TIPS, 219 by ES. The cumulative proportions of events at 2 years were: rebleeding 43%(TIPS)vs. 67.5%(ES;p < 0.0001); survival 55.5% vs.67.5%(p=0.3371);encephalopathy 53.3% vs. 16.1%(p <0.0001).Nine potential prognostic markers were analyzed by Cox's models.The results of the analysis are reported in the table.Conclusions:TIPS patients show significantly fewer rebleeds and significantly more encephalopathy than ES patients. Albumin, PT,bilirubin, Child class and days between bleeding and treatment are indicators of poor prognosis for TIPS patients. PT predicts poor outcomes in ES patients.

End-point	TIPS		ES	
	prognostic variable	p	prognostic variable	p
Rebleeding	albumin	=0.017	PT	=0.019
	PT	=0.021		
Death	Child class	=0.04	PT	<0.0001
	PT	=0.026		
Encephalop.	Child class	<0.0001	PT	=0.012
	bilirubin	=0.0003		
	days between bleed and Rx	=0.012		

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LIGATION VS PROPRANOLOL FOR PRIMARY PROPHILAXIS OF VARICEAL BLEEDING USING A MULTIPLE BAND LIGATOR AND OBJECTIVE MEASUREMENTS OF TREATMENT ADEQUACY: PRELIMINARY RESULTS.

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BACKGROUND: Propranolol is the accepted treatment for primary prophylaxis of variceal bleeding, althought as much as 40% might not have a decrease in portal pressure even at doses with clinical response. Sclerotherapy seems to be useful only in patients with large varices; however, this procedure has complications. Ligation is as useful but with less complications and so, could become the procedure of choice. MATERIAL AND METHODS: All patients with no bleeding history and high risk, large varices were included. Patients with contraindications to propranolol were excluded. They were randomly assigned to: group 1: ligation and group 2: propranolol. Baseline portal pressure was measured by the transjugular approach in all and to confirm adequate response in group 2. Ligation was done until erradication as ascertained by endoscopic ultrasound, while propranolol was administered in increasing dose until heart rate was below 60X' or a 20% decrease from baseline occurred. Variables analyzed were: age, gender, Child-Pugh stage, baseline portal pressure, # of bands to erradication, # sessions to erradication, propranolol dose, complications, rebleeding, death, variceal reformation and withdrawal from either group. Comparisons were made using students T test, Chi square or Fischer's