PO Box 2345, Beijing 100023, China
www.wjgnet.com
wjg@wjgnet.com

ELSEVIER

World J Gastroenterol 2005;11(14):2067-2071
World Journal of Gastroenterology ISSN 1007-9327

• *LIVER CANCER* •

Hepatic resection for hepatocellular carcinoma in end-stage renal disease patients: Two decades of experience at Chang Gung Memorial Hospital

Chun-Nan Yeh, Wei-Chen Lee, Miin-Fu Chen

Chun-Nan Yeh, Wei-Chen Lee, Miin-Fu Chen, Department of General Surgery, Chang Gung Memorial Hospital, Chang Gung University, Taoyuan, Taiwan, China
Correspondence to: Dr. Chun-Nan Yeh, Department of General Surgery, Chang Gung Memorial Hospital, 5 Fu-Hsing Street, Kwei-Shan, Taoyuan, Taiwan, China. ycn@adm.cgmh.org.tw
Telephone: +886-3-3281200-3219 Fax: +886-3-3285818
Received: 2004-10-13 Accepted: 2004-12-23

Key words: HCC; ESRD

Yeh CN, Lee WC, Chen MF. Hepatic resection for hepatocellular carcinoma in end-stage renal disease patients: Two decades of experience at Chang Gung Memorial Hospital. *World J Gastroenterol* 2005; 11(14): 2067-2071
http://www.wjgnet.com/1007-9327/11/2067.asp

Abstract

AIM: Hepatocellular carcinoma (HCC) is a common disease in Taiwan. The prevalence of viral hepatitis infection and the subsequent development of HCC are well known to be higher in patients with end-stage renal disease (ESRD) requiring hemodialysis (HD) or peritoneal dialysis (PD) than among the general population. However, information on hepatic resection for ESRD-HCC patients is limited.

METHODS: The clinical features of 26 ESRD-HCC patients who underwent hepatic resection from 1982 to 2001 were retrospectively reviewed. Meanwhile, the clinicopathological features and the outcome of 1 198 HCC patients without ESRD undergoing hepatic resection were used for comparison.

RESULTS: Of 1 224 surgically resected HCC patients, 26 (4.2%) were ESRD-HCC. Univariate analysis revealed more associated disease, more physical signs of anemia and postoperative complications, lower hemoglobin, platelet, α-fetoprotein, elevated blood urea nitrogen (BUN) and creatinine levels, smaller tumors, lower HBsAg positivity, higher HCV positivity, and longer hospital stays in the ESRD-HCC group compared with the HCC group. Furthermore, multivariate stepwise logistic regression analysis revealed that elevated BUN and creatinine levels were the only two independently significant factors in the patients in the ESRD-HCC group. Overall and disease-free survival rates were similar between the ESRD-HCC and HCC groups.

CONCLUSION: Elevated BUN and creatinine were the only two main independent factors differentiating ESRD-HCC from HCC patients. ESRD should not be a contraindication of hepatic resection in HCC patients; however, careful operative techniques and perioperative care are crucial to achieving lower morbidity and mortality. Comparable overall survival and disease-free survival can be achieved in selected ESRD-HCC patients undergoing hepatic resection when compared with conventional HCC patients.

INTRODUCTION

Hepatocellular carcinoma (HCC) is a common disease in Taiwan, with an annual age-adjusted prevalence of 28.7/100 000 population. HCC is the leading cause of cancer-related death among men, and second among women in Taiwan[1].

Although liver transplantation provides an alternative option for the surgical management of HCC, partial hepatic resection remains the mainstay of treatment. With improvements in surgical techniques and perioperative care, surgical mortality rates in HCC patients receiving hepatectomy have recently reduced significantly[2]. The prevalence of viral hepatitis infection and the subsequent development of HCC are well known to be higher in patients with end-stage renal disease (ESRD) requiring hemodialysis (HD) or peritoneal dialysis (PD) than among the general population[3,4]. Such patients are usually immunocompromised and have various degrees of associated coagulopathy[4-6]. Because hemorrhage, infection, and liver failure are the main causes of death after liver resection, HCC resection should be particularly risky for patients with ESRD[7]. However, few reports exist on liver resection for HCC in such patients[3,6,7]. This study attempted to determine the outcome of liver resection for HCC in ESRD patients.

MATERIALS AND METHODS

From 1982 to 2001, 1 224 consecutive HCC patients underwent surgery at the Department of Surgery, Chang Gung Memorial Hospital, Taipei, Taiwan. Among them, 26 HCC patients (4.2%) suffering ESRD treated with HD, and/or continuous ambulatory peritoneal dialysis (CAPD) undergoing curative surgery were classified as ESRD-HCC group, while the remaining 1 198 patients were classified as HCC group. Sixty-seven patients were excluded from the survival analysis due to incomplete follow-up records. Totally

Table 1 Demographic data of 1 224 HCC patients undergoing hepatectomy with and without ESRD

	ESRD–HCC (%) (n = 26)	HCC (%) (n = 1 198)	P
Age (yr)	53.4±13.2	54.3±13.7	0.748
Gender (M:F)	22:4	937:261	0.433
Associated disease	19 (73.1)	406 (33.9)	0.0001
Symptoms (+)	17 (65.4)	799 (66.7)	0.889
Physical findings (+)	13 (50.0)	289 (24.1)	0.002
HBsAg (+)	11 (42.3)	782 / 1 101 (71.0)	0.002
Anti-HCV Ab (+)	15 (62.5)	314 / 854 (36.8)	0.01
Dual infection (+)	2 / 23 (8.7)	99 / 816 (36.8)	1.0
Associated cirrhosis (+)	14 (53.8)	647 / 1 187 (54.5)	0.947
child-pugh grade			
A	19 (76.0)	1 014 (89.5)	
B+C	6 (24)	119 (10.5)	0.055

M: male; F: female; HBsAg: hepatitis B surface antigen; HCV: hepatitis C virus; Ab: antibody.

1 157 patients were enrolled in this study for survival analysis. In this study, 66 HCC patients (including three ESRD-HCC patients) died within one month after surgery (surgical mortality rate 5.4%; 66/1 224). Laboratory tests were performed on the day before surgery. Differences in demographics, symptomatology, physical examination, laboratory data, presence of cirrhosis, operative findings, and pathological features between the two groups were compared. Clinicopathological features were conditioned as presence or absence; resection margin less than 1 cm *vs* a margin of more than 1 cm; and low histological grading *vs* high grade. Resections included segmentectomy, lobectomy, extended lobectomy, subsegmentectomy, and wedge resection. Segmentectomy is a resection of one of the four segments (lateral, medial, anterior, or posterior) of the liver as classified by Healey and Schroy. Subsegmentectomy is a resection of a Couinaud segment. Histopathological findings of HCC were divided into four grades according to Edmondson and Stainer's system. Grades I and II were conditioned as low-grade, and grades III and IV as high-grade HCC (described as previously)[8].

Table 2 Laboratory data of 1 224 HCC patients undergoing hepatectomy with and without ESRD

	ESRD–HCC (%) (n = 26)	HCC (%) (n = 1 198)	P
AFP (ng / mL)	2 143.7±1 0365.5	6 520.9±9 9070.2	0.825
AFP>400 ng / mL	2 / 25 (8.0)	392 / 1 098 (35.7)	0.003
Hemoglobin (g / dL)	10.6±2.5	13.0±2.1	0.0001
WBC (/ μL)	6 284.6±3 031.0	7 467.6±7 956.4	0.449
Platelet (10^3 / μL)	134.7±77.0	179.4±99.2	0.023
PT / PT (normal control)	0.85±1.6	0.96±1.9	0.778
INR (%)	1.10±0.16	1.10±0.18	0.953
Albumin (g / dL)	3.70±0.67	3.90±0.62	0.115
Bilirubin (direct) (mg / dL)	0.30±0.14	0.51±1.16	0.588
Bilirubin (total) (mg / dL)	0.80±0.36	1.12±1.27	0.207
BUN (mg / dL)	54.9±26.9	15.5±7.1	0.0001
Creatinine (mg / dL)	6.64±4.01	1.21±1.69	0.0001
AST (IU / L)	63.5±55.5	72.6±96.0	0.631
ALT (IU / L)	46.6±51.1	63.9±71.0	0.236
ALP (IU / L)	101.5±45.2	114.7±295.6	0.827
ICG 15 (%)	19.4±15.6	14.5±13.9	0.143

AFP: α-fetoprotein; PT: prothrombin time; INR: international normalized ratio; BUN: blood urea nitrogen; AST: aspartate aminotransferase; ALT: alanine aminotransferase; ALP: alkaline phosphatase; ICG 15: indocyanine green retention rate at 15 min.

Before admission for liver resection, one patient received CAPD and the remaining 25 patients underwent regular HD thrice weekly. Etiologies diagnosed in the 26 patients were as follows: idiopathic nephropathy (12), diabetic nephropathy (5), gouty nephropathy (2), nephrolithiasis (1), nephrotic syndrome (1), gouty nephropathy (1), malignancy (transitional cell carcinoma) associated nephropathy (1), hypertensive nephropathy (2), and polycystic kidney disease (1). The duration of dialysis ranged from 2 to 152 mo (median/mean: 37/46.3 mo). The patient who underwent CAPD shifted to HD about 1 wk before surgery. HD was conducted on the day before surgery, and then continued post-surgery was being conducted on alternate days, starting from the first day of post-surgery. CAPD was resumed for one patient after discharge.

Statistical analysis

All data are presented as percentage of patients or mean with standard deviation. Numerical data were compared by independent student two-sample t tests. Nominal data were compared by Pearson χ^2 test, Fisher exact test, or multiple forward stepwise logistic regression when appropriate. Survival was calculated and plots constructed according to the Kaplan-Meier method and compared with a log-rank test between groups. All statistical analyses were performed using the SPSS computer software package (Version 10.0, Chicago, IL). A value of $P<0.05$ was considered significant.

RESULTS

The ESRD-HCC group contained 22 men and 4 women, with a mean age of 53.4±13.2 years (range, 30-83 years). The ESRD-HCC and HCC groups displayed similar age distributions and gender ratios (Table 1). However, associated disease and anemia (hemoglobin <10 gm/dL) were more common in the ESRD-HCC group than the HCC group (Tables 1 and 4). Hypertension was the most commonly associated disease (10/19; 52.6%), followed by diabetes mellitus (DM; 8/19; 42.1%) (Table 4). Notably, ESRD-HCC patients displayed a lower percentage of positive

Table 3 Operative, macroscopic, and microscopic findings of HCC patients with and without ESRD

	ESRD–HCC (%) (n = 26)	HCC (%) (n = 1 198)	P
Major hepatectomy	17 / 26 (65.4)	603 / 1 198 (50.3)	0.129
Blood loss (cc)	955.8±771.2	1 358.6±1 593.3	0.199
Blood transfusion (cc)	462.0±580.1	1 037.9±2 261.9	0.204
Tumor size (cm)	4.1±2.0	6.2±4.5	0.0001
Tumor size >5 cm	6 / 26 (23.1)	545 / 1 171 (46.5)	0.018
Grading (Edmondson and Stainer)			
Low-grade (I+II)	10 / 25 (40.0)	504 / 948 (53.2)	
High-grade (III+IV)	15 / 25 (60.0)	444 / 948 (46.8)	0.193
Capsule formation (+)	16 / 21 (76.2)	676 / 1 012 (66.8)	0.365
Capsule invasion (+)	8 / 15 (53.3)	359 / 625 (57.4)	0.751
Macroscopic vascular invasion (+)	8 / 24 (33.3)	431 / 1 150 (37.5)	0.678
Satellite lesions (+)	5 / 25 (20.0)	336 / 1 155 (29.1)	0.321
Resection margin >1 cm	12 / 23 (52.2)	373 / 1 051 (35.5)	0.099
Rupture (+)	3 / 26 (11.5)	140 / 1 167 (12.0)	0.943
Complication	11 / 26 (42.3)	240 / 1 198 (20.0)	0.005
Hospital stay (d)	26.8±11.7	21.7± 12.7	0.046
Mortality	3 / 26 (11.5)	63 / 1 198 (5.3)	0.161

Table 4 Associated disease, morbidity, and postoperative mortality of 26 ESRD–HCC and 1 198 HCC patients treated with hepatectomy

	ESRD–HCC (n = 26)		HCC (n = 1 198)
Associated disease	19 (73.1%)	Associated disease	406 (33.9%)
ESRD only	7	Peptic ulcer	121
Hypertension	10	DM	111
DM	8	Hypertension	88
Heart disease	3	DM+hypertension	42
TCC	1	DM+peptic ulcer	20
Peptic ulcer	6	Heart disease	31
		CVA	11
		Biliary tract disease (GB stone or CBD stone or IHD stone)	27
		Lung disease	27
		Others	71
Morbidity	11 (42.3%)	Cause of mortality	66 (5.3%)
Pleural effusion	4	Hepatic failure	12
Ascites	2	Infection-induced hepatic failure	10
Jaundice	1	Intra-abdominal bleeding	23
Pneumonia	1	Cholangitiitis	1
Intra-abdominal abscess	1	Bile leakage	1
Wound infection	1	ARDS	2
Fever	1	EV bleeding	2
Cause of mortality	3 (11.5%)	Peptic ulcer bleeding	3
Sepsis	2	Combine EV and peptic ulcer bleeding	1
Pulmonary embolism	1	Renal failure	4
		Pneumonia / pulmonary embolism	1 / 1
		VT / heart failure	1 / 1
		Ischemic bowel / hollow organ perforation	1 / 1
		DIC	1

TCC: transitional cell carcinoma; DM: diabetes mellitus; CVA: cerebrovascular disease; GB: gallbladder; CBD: common bile duct; IHD: intrahepatic duct; ARDS: adult respiratory distress syndrome; EV: esophageal variceal; VT: ventricular tachycardia; DIC: disseminated intravascular coagulopathy.

hepatitis B and higher percentage of hepatitis C compared to the HCC group. Although rates of underlying liver cirrhosis did not differ significantly between the two groups, ESRD-HCC patients tended to have lower percentage of Child-Pugh grade A (P = 0.055) (Table 1).

Table 2 displays the results of all preoperative laboratory tests. Levels of AFP, hemoglobin, platelet, blood urea nitrogen (BUN), and creatinine differ between the two groups.

Table 3 lists the operative, macroscopic, and microscopic findings. Patients in the ESRD-HCC group displayed similar extent of hepatectomy, blood loss, and blood transfusion to those in the HCC group. Notably, tumor size was smaller in the ESRD-HCC group than the HCC group (P = 0.0001). However, the percentages of low-grade and high-grade HCC were similar in both groups. Generally, the tumors in the ESRD-HCC group had similar capsule formation, capsular invasion, vascular invasion, satellite lesions, rupture rate, and clearance margins to those in the HCC group (Table 3). Table 4 displays the causes of operative mortality of ESRD-HCC and HCC patients. Overall mortality rate was 5.4% (66/1 224). The mortality rates of the ESRD-HCC (11.5%) patients undergoing hepatic resection are higher than the HCC groups (5.3%), although it is not statistically significant (P = 0.161). Meanwhile, more complications and longer stay at hospital were noted in the ESRD-HCC patients than the HCC patients (P = 0.005 and 0.046).

Table 5 Univariate and multiple forward stepwise logistic regression analysis of clinicopathological features in 1 224 HCC patients after hepatectomy between ESRD and non-ESRD groups

	Univariate analysis P	Multivariate logistic regression analysis P
Associate disease	0.001	NS
Presence of physical findings	0.002	NS
Positive HBsAg	0.002	NS
Positive anti-HCV Ab	0.002	NS
Platelet<150 000 / mL	0.011	NS
Hb<10 g / dL	0.0001	NS
BUN>30 mg / dL	0.0001	0.0001
Cr>1.5 mg / dL	0.0001	0.002
AFP>400 ng / L	0.003	NS
Tumor size<5 cm	0.018	NS
Hospital stay>21 d	0.035	NS
Complication	0.005	NS

HBsAg: hepatitis B surface antigen; HCV: hepatitis C virus; Ab: antibody; Hb: hemoglobin; BUN: blood urea nitrogen; Cr: creatinine; AFP: α-fetoprotein

Univariate analysis showed that associated disease, physical signs of anemia, lower hepatitis B positivity, higher hepatitis C positivity, lower hemoglobin and platelet count, elevated BUN, creatinine and AFP levels, smaller tumor size, more complications, and longer stay at hospital were associated with ESRD-HCC. However, multivariate logistic regression analysis showed that elevated BUN and creatinine were the only two independent factors differentiating ESRD-HCC from HCC (Table 5).

All the 1 157 patients who underwent hepatic resection were followed regularly until death. The duration of follow-up for 26 ESRD-HCC and 1 131 HCC patients ranged from 0.01 to 97.6 mo (median = 15.0 mo) and 0.01 to 213.5 mo (median = 14.6 mo), respectively. Table 6, Figures 1A and B display overall and disease-free survival for the ESRD-HCC and HCC groups. The 1-, 3-, and 5-year overall survival rates were 82.0%, 38.1%, 38.1% in the ESRD-HCC group and 70.6, 48.6, 34.8% in the HCC group, respectively. Moreover, the 1-, 3-, and 5-year disease-free survival rates were 63.1%, 49.1%, and 16.4% in the ESRD-HCC group, and 55.2%, 35.4%, 26.9% in the HCC group, respectively. Notably, the patients in the ESRD-HCC group had similar overall and disease-free survival to those in the HCC group.

DISCUSSION

Contrary to Cheng's report, ESRD-HCC patients displayed comparable clinicopathological features to HCC patients with exception of displaying lower hemoglobin and higher serum creatinine levels[7]. This study demonstrated that ESRD-HCC patients undergoing hepatectomy differed from HCC patients in several respects. ESRD-HCC patients undergoing hepatectomy had higher rate of underlying associated disease, as well as physical findings of anemia,

Table 6 Prognosis of HCC patients undergoing hepatectomy with and without ESRD

	ESRD–HCC (%) (n = 26)	HCC (%) (n = 1 131)	P
Overall survival (mo)			
mean	47.9	63.3	
Median	23.6	32.8	
95%CI of mean	27.3; 68.4	55.7; 71.0	
Log-rank			0.7034
DFS (mo)			
mean	35.9	52.0	
Median	14.8	15.5	
95%CI of mean	17.0; 54.7	43.7; 60.3	
Log-rank			0.6123

CI: confidence interval; DFS: disease-free survival.

lower positivity of hepatitis B infection, and higher positivity of hepatitis C infection. Hypertension is the disease most commonly associated with ESRD, followed by DM. Hepatitis B and C are two common pathogens causing chronic hepatitis in patients with ESRD. The acceptance of hepatitis B surface antigen screening has led the infected patients being identified and isolated over the past 20 years. Consequently, hepatitis B is now encountered less frequently in dialysis units. However, while hepatitis B has become less problematic, hepatitis C has been recognized as a significant problem since 1979. The prevalence of anti-HCV in HD patients is quite variable, ranging from 5 to over 50%[9]. In Taiwan, the rate of anti-HCV in HD patients is 30.5% [10], and is significantly lower in patients with CAPD[11]. Anti-HCV positivity is associated with previous blood transfusion, mode of therapy, and duration of HD.

ESRD-HCC patients undergoing hepatectomy exhibited lower hemoglobin level than HCC patients, explaining the higher positivity for physical findings of anemia in ESRD-HCC patients. Anemia can be a complication of the HD procedure itself, with its associated blood loss. ESRD-HCC patients also had lower platelet count than HCC patients. Reduced platelet counts were more common in patients on dialysis, particularly in HCV-positive HD patients, and the failure of megakaryocyte production by the bone marrow is a fundamental cause of this platelet reduction in both HD and CAPD patients[12].

ESRD-HCC patients exhibited lower AFP level and significantly lower percentage of AFP >400 ng/mL compared with HCC patients without ESRD. That ESRD-HCC patients have lower percentage of HBsAg positivity and smaller tumor size may explain the lower AFP values[8,13]. From the world literature on factors affecting the prognosis of surgically treated patients, previous European and Japanese reports emphasize the importance of preoperative AFP value[14,15]. The Italian group proposed the CLIP scoring system for the staging for HCC based partly on AFP value[14]. The specific reason for raised AFP level worsening the prognosis is uncertain. AFP may be a unique biological variable expressing grade of malignancy, and has suppressive effects on the immunologic reaction directed against tumor cells[16]. Regarding tumor markers, several investigations have demonstrated that AFP level is not influenced by uremic status and maintains its specificity for tumor monitoring in uremic status[17]. ESRD-HCC patients had smaller tumors and lower percentage of tumor size >5 cm compared with HCC patients without ESRD. HCC screening for chronic hepatitis B and hepatitis C carriers in endemic areas using AFP and/or abdominal ultrasound could identify tumors, especially smaller ones, explaining the observation. Our previous study demonstrated that HCV patients had smaller tumors[18]. We also demonstrated that HCC patients with larger tumor size had higher percentages of positive hepatitis B infection and lower percentage of hepatitis C infection. Meanwhile, overall survival and disease-free survival for HCC patients undergoing hepatic resection with tumor larger than 10 cm is worse than for those with tumor less than 10 cm, which is significantly influenced by the high value of AFP[8]. Smaller tumor size, lower AFP level, and significantly lower percentage of AFP >400 ng/mL in ESRD-HCC patients may partly explain no significant survival difference to HCC patients.

This study observed a higher prevalence of postoperative complications among ESRD-HCC patients after hepatectomy, explaining the longer hospital stays and higher mortality rate of ESRD-HCC patients. Notably, a higher percentage of HCV infection, Child-Pugh grade, and more associated disease may partially contribute to the more eventful postoperative courses of ESRD-HCC patients compared to HCC patients. Our previous study demonstrated that HCV-related HCC patients were older, and tended to have severe, and progressive liver disease[18]. Generally, septic problems occur most frequently with advanced cirrhosis and contribute heavily to the increased mortality. The increased infection rate may be partially explained by the

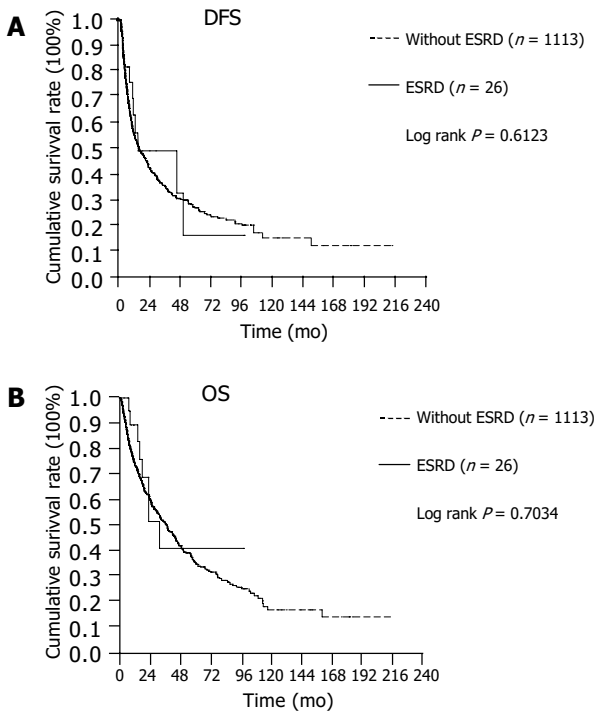

Figure 1 A: Disease-free survival of 26 HCC patients with ESRD undergoing hepatectomy *vs* 1 131 HCC patients without ESRD undergoing hepatectomy; B: Overall survival of 26 HCC patients with ESRD undergoing hepatectomy *vs* 1 131 HCC patients without ESRD undergoing hepatectomy.

impairment of Kupffer cell function, which reduces intravascular clearance of the enteric organism[19]. Additionally, ascitic fluid may provide an ideal growth medium for bacterial contaminants released during cholecystectomy[19]. Overall, the relative risk of septic complications depends on the severity of cirrhosis. Numerous investigations have correlated the prevalence of sepsis with the patient's Child-Pugh classification[19]. This study finds that pleural effusion and ascites are the two most common complications after hepatic resection. For hepatic surgeons, careful operative techniques and perioperative care are crucial to achieving an uneventful postoperative course and preventing postoperative wound infection and intra-abdominal abscess, even mortality.

As for prognosis, comparable overall survival and disease-free survival can be achieved in selected ESRD-HCC patients undergoing hepatic resection when compared to conventional HCC patients in this study. Since the first combined liver-kidney transplant was proposed in 1983[20], this procedure has gained increasing popularity for liver failure and irreversible renal insufficiency[20]. To the best of our knowledge, no report regarding combined liver-kidney transplant for ESRD-HCC patients is noted in the literature.

In summary, elevated BUN and creatinine values were the only two independent factors differentiating ESRD-HCC from HCC patients. ESRD should not be a contraindication of hepatic resection in HCC patients; however, careful operative techniques and perioperative care are crucial to achieving lower morbidity and mortality. Comparable overall survival and disease-free survival to conventional HCC patients can be achieved in selected ESRD-HCC patients undergoing hepatic resection.

REFERENCES

1 Department of Health, Executive Yuan, Republic of China. Annual report of cancer registration, 2001

2 **Fan ST**, Lo CM, Liu CL, Lam CM, Yuen WK, Yeung C, Wong J. Hepatectomy for hepatocellular carcinoma: Toward zero hospital deaths. *Ann Surg* 1999; **229**: 322-330

3 **Hayashi H**, Ohtake Y, Kashima T, Irie Y, Murata M, Hayashi H, Kobayashi S, Okuda K. Hepatocellular carcinoma among hemodialysis patients infected with hepatitis C virus-early evolution and rapid prognosis. *Clin Nephrol* 1999; **51**: 321-323

4 **Mailloux LU**, Bellucci AG, Wilkes BM, Napolitano B, Mossey RT, Lesser M, Bluestone PA. Mortality in dialysis patients: analysis of the cause of death. *Am J Kidney Dis* 1991; **18**: 326-335

5 **Remuzzi G.** Bleeding in renal failure. *Lancet* 1988; **1**: 1205-1208

6 **Yamagata M**, Kanematsu T, Matsumata T, Nishizaki T, Utsunomiya T, Sugimachi K, Okuda S. Possibility of hepatic resection in patients on maintenance hemodialysis. *Hepatogastroenterology* 1993; **40**: 249-252

7 **Cheng SB**, Wu CC, Shu KH, Ho WL, Chen JT, Yeh DC, Liu TJ, P'eng FK. Liver resection for hepatocellular carcinoma in patients with end-stage renal failure. *J Surg Oncol* 2001; **78**: 241-247

8 **Yeh CN,** Lee WC, Chen MF. Hepatic resection and prognosis for patients with hepatocellular carcinoma larger than 10 cm: Two Decades of Experience at Chang Gung Memorial Hospital. *Ann Surg Oncol* 2003; **10**: 1070-1076

9 **Huang CC.** Hepatitis in patients with end-stage renal disease. *J Gastroenterol Hepatol* 1997; **12**: S236-241

10 **Hung CC.** Dialysis therapy in Taiwan: 1995 National Surveillance Report. *J Nephrol ROC* 1995; **9**: 71-83

11 **Huang CC,** Wu MS, Lin DY, Liaw YF. The prevalence of hepatitis C virus antibodies in patients treated with continuous ambulatory peritoneal dialysis. *Perit Dial Int* 1992; **12**: 31-33

12 **Paganini EP.** Overview of anemia associated with chronic renal disease: primary and secondary mechanism. *Seminars In Nephrol* 1989; **9**(1 Suppl 1): 3-8

13 **Nomura F,** Ohnishi K, Tanabe Y. Clinical features and prognosis of hepatocellular carcinoma with reference to serum alpha-fetoprotein levels. Analysis of 606 patients. *Cancer* 1989; **64**: 1700-1707

14 The liver cancer study group of Japan. Primary liver cancer in Japan: clinicopathological features and results of surgical treatment. *Ann Surg* 1990; **211**: 278-287

15 The Cancer of the Liver Italian Program (CLIP) investigators. A new prognostic system for hepatocellular carcinoma. A retrospective study of 435 patients. *Hepatology* 1998; **28**: 751-755

16 **Yachnin S,** Soltani K, Lester EP. Further studies on the mechanism of suppression of human lymphocyte transformation by human alpha-fetoprotein. *J Allergy Clin Immunol* 1980; **65**: 127–135

17 **Odagiri E**, Jibiki K, Takeda M, Sugimura H, Iwachika C, Abe Y, Kihara K, Kihara Y, Itou M, Nomura T. Effect of hemodialysis on the concentration of the seven tumor markers carcinoembryonic antigen, alpha-fetoprotein, squamous cell carcinoma-related antigen, neuron-specific enolase, CA 125, CA 19-9 and CA 15-3 in uremic patients. *Am J Nephrol* 1991; **11**: 363-368

18 **Chen MF,** Jeng LB, Lee WC. Surgical results in patients with hepatitis virus-related hepatocellular carcinoma in Taiwan. *World J Surg* 2002; **26**: 742-747

19 **Mansour A,** Watson W, Shayani V, Pickelman J. Abdominal operations in patients with cirrhosis: Still a major surgical challenge. *Surgery* 1997; **122**: 730-735

20 **Margreiter R**, Kramar R, Huber C, Steiner E, Niederwieser D, Judmaier G, Vogel W. Combined liver and kidney transplantation. *Lancet* 1984; **12**: 1077-1078

21 **Jeyarajah DR**, McBride M, Klintmalm GB, Gonwa TA. Combined liver-kidney transplantation: what are the indications? *Transplantation* 1997; **64**: 1091-1096

Science Editor Guo SY **Language Editor** Elsevier HK