J Med Sci 2013;33(6):311-319
http://jms.ndmctsgh.edu.tw/3306311.pdf
DOI:10.6136/JMS.2013.33(6).311

A Comparison of Outcomes between Liver Transplant Recipients in China and those in Taiwan

Teng-Wei Chen[1], Chih-Yung Yu[2], Heng-Cheng Chu[3], De-Chuan Chan[1], Guo-Shiou Liao[1] , and Chung-Bao Hsieh[1,4*]

[1]Division of General Surgery, Department of Surgery; [2]Department of Radiology; [3]Division of Gastroenterology, Department of Internal medicine; [4]Division of Organ Transplantation, Department of Surgery, Tri-Service General Hospital, National Defense Medical Center, Taipei, Republic of China

Background: The outcome of liver transplantation in Taiwan and overseas has not been compared directly. We investigated differences in outcomes between liver transplant recipients in China and those in Taiwan. **Materials and Methods:** Ninety-two patients who underwent liver transplantation in China and were subsequently being followed at the Tri-Service General Hospital (TSGH; China group; CG) were compared with 107 patients who received transplants at TSGH (Taiwan group; TG). Donor and recipient characteristics, complications, and survival were analyzed. Survival was calculated using the Kaplan–Meier method, and univariate analysis was tested by the log-rank test. Then, regression analysis was performed using the Cox proportional hazard model. **Results:** The number of patients with hepatocellular carcinoma (HCC) beyond the Milan and University of California, San Francisco criteria was significantly higher in the CG than in the TG. The rates of HCC recurrence, intrahepatic biliary strictures, and mortality were also higher in the CG than in the TG. Univariate analysis revealed significant differences in 8 parameters between survivors and non-survivors, and Cox regression analysis further identified psychosocial problems, post-transplant de novo malignancy, HCC recurrence, and graft failure as mortality predictors. The overall survival rate was significantly higher in the TG than in the CG, with the former group showing a trend of greater mean survival duration. However, differences in survival were not significant after adjusting for risk factors. **Conclusion:** The outcomes of patients receiving livers donated after cardiac death may be comparable; however, patients with advanced HCC should not seek transplantation without appropriate pre-transplant tumor treatments.

Key words: liver transplantation, survival, brain death, donation after cardiac death, down-stage therapy

INTRODUCTION

Liver transplantation is considered a curative treatment for most end-stage liver diseases (ESLDs) and selected cases of hepatocellular carcinoma (HCC).[1] In Taiwan, organ transplantation has become acceptable among the general population, but a shortage of deceased donors remains a limiting factor. The introduction of living donor liver transplantation (LDLT) has decreased the dependence on deceased donors and the waiting time for many patients.

However, LDLT is not without risks to the donor. A report published in 2008 revealed that, of an estimated 14,000 LDLTs performed worldwide, the prevalence of donor death was 0.1%–0.3% and could reach 0.5% if the right hemi-liver was used.[2] Consequently, the use of LDLT is still not widespread; therefore, some patients travel to China to undergo liver transplantation. The law in Taiwan does not allow doctors to refer their patients to China for liver transplantation; therefore, patients must arrange for this procedure themselves. Because this venture involves significant cost, most patients who go to China for liver transplantation tend to be financially stable.

In Taiwan, almost all deceased donors are brain dead. Because of the shortage of donors, if a patient receives a poor graft, he/she has little chance to obtain a second one. Livers donated after cardiac death are not been used

Received: December 17, 2012; Revised: June 7, 2013; Accepted: June 18, 2013
*Corresponding author: Chung-Bao Hsieh, Division of Organ Transplantation, Department of Surgery, Tri-Service General Hospital, National Defense Medical Center, No. 325, Sec. 2, Cheng-gong Road, Taipei 114, Taiwan, Republic of China. Tel: +886-2-87927191; Fax: +886-2-87927372; E-mail: albert0920@yahoo.com.tw

at our hospital (Tri-Service General Hospital (TSGH), National Defense Medical Center Taipei, Taiwan), whereas in China, almost all livers from deceased donors are donated after cardiac death (i.e., non-heart-beating donors)[3] in the study period.

This study aimed to compare the outcomes of liver transplantation between recipients in Taiwan and those in China to identify significant risk factors that can influence the survival of these recipients.

MaterialS AND METHODS

Patients

Ninety-two adult patients (81 males) who received a liver transplant in China between December 2001 and May 2008 and were being followed up at the TSGH in Taiwan [China group; (CG)] were included in this study. During the same period, 107 adult patients (79 men) received liver transplants at the TSGH [Taiwan group; (TG)]. Patients in the CG received liver transplants donated after cardiac death and returned to Taiwan for follow-up after hospital discharge. They were followed up and managed like any other liver transplant patient who underwent this procedure at the TSGH. In the TG, 65 patients underwent LDLT while 42 underwent deceased donor liver transplantation (DDLT). Patients who died during surgery, those aged <18 years, and those who continued their follow-up at other hospitals were excluded from the study. During the same period, the waiting list for liver transplantation at the TSGH was analyzed, including patients who received transplants, those who dropped out, and those still on the list. The definition of drop-out was patients who died or developed extrahepatic HCC metastases while waiting for a transplant. Most patients in the CG were not referred from our hospital; therefore, the surgical mortality rate in this group could not be measured. The CG included only those patients who underwent transplantation in China, returned to Taiwan, and underwent follow-up at the TSGH. The date of final follow-up was June 5, 2009.

This research was approved by the institutional review board of the TSGH (TSGHIRB 100-05-220).

Statistical analysis

Donor characteristics, recipient characteristics, complications encountered, and survival were analyzed in the 2 groups. Continuous data were tested using Student's *t*-test, while categorical data were tested using the chi-square or Fisher's exact test. Univariate analysis of survival was tested by the log-rank test. Factors identified to be significant predictors of survival were analyzed by regression analysis using the Cox proportional hazard model. A P value of <0.05 was considered statistically significant. All statistical analyses were performed using SPSS for Windows 15.0 (SPSS, Inc., Chicago, IL, USA).

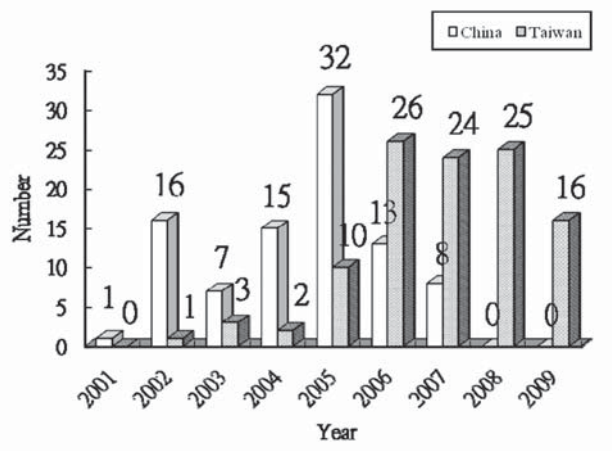

Fig. 1 Annual number of liver transplantations in the China group and Taiwan group

RESULTS

Patient distribution

Most of the liver transplants undertaken in China were performed between 2002 and 2006; the number of procedures peaked in 2005 and tapered off in 2008. On the other hand, the number of transplants in the TG increased gradually from only 1 patient in 2002 to >20 patients since 2006, with a projected increase to >30 patients in 2009 (Fig. 1). The percentage of LDLTs increased in later years, once this procedure became more acceptable in Taiwan.

Clinicopathological characteristics

There was no significant difference in recipient age between the 2 groups, whereas the male-to-female ratio was significantly higher in the CG than in the TG.

Hepatitis B virus (HBV) infection was the most frequent etiology of ESLD in both groups. The number of patients with HCC was significantly higher in the CG than in the TG (69.6% *vs*. 40.2%, P = 0.03), whereas the TG included more patients with alcoholic liver disease compared with the CG (16.8% *vs*. 6.5%, P = 0.04). Furthermore, the number of patients with HCC beyond the Milan and University of California, San Francisco (UCSF) criteria was significantly higher in the CG than

Table 1 Characteristics of donors and recipients, complications, and outcomes of liver transplantation in the China and Taiwan groups

	China group (n = 92)	Taiwan group (n = 107)	*P*
Donor characteristics			
Non-heart-beating donor	92	0	
Living + split donor	0	65	
Cadaver donor	0	42	
Recipient characteristics			
Age	51.5±10.3	52.4±9.8	0.55
F/M	11/81	28/79	0.02
Etiology			
HBV	69	69	0.09
HCV	16	28	0.08
Alcoholic	6	18	0.04
Other	1	7	0.13
HCC	64	45	0.03
HCC criteria			
Milan criteria (fit/nonfit)	19/45	34/11	<0.001
UCSF (fit/nonfit)	25/39	35/10	<0.001
Complications			
Biliary complications	14	25	0.16
Surgical complications	7	14	0.16
TB infection	2	4	0.69
Renal complications	6	6	0.99
Vascular complications	2	1	0.6
Graft failure	6	3	0.31
Psychosocial problems	2	11	0.023
Acute rejection	13	14	0.84
De novo malignancy	3	4	0.99
Re-exp lap	14	11	0.39
HCC recurrence	32	5	<0.001
Outcome			
Survival/death	47/45	91/16	<0.001
duration	50.0±3.7	53.9±3.4	0.35

HBV, hepatitis B virus infection; HCV, hepatitis C virus infection; alcoholic, alcoholic-related liver cirrhosis; other, except virus or alcoholic-related liver cirrhosis and HCC; HCC, hepatocellular carcinoma; TB, tuberculosis; re-exp lap, second exploratory laparotomy after liver transplantation; UCSF, University of California, San Francisco.

in the TG. Of the 64 HCC patients in the CG, 45 (70%) were beyond the Milan criteria, and 39 of these were also beyond the UCSF criteria. The other indications for liver transplantation in the CG included cholangiocarcinoma (n = 1). In the TG, the other indications included Wilson's disease (n = 1), mixed HCC and cholangiocarcinoma (n = 2), biliary atresia (n = 1), cryptogenic cirrhosis (n = 1), acute hepatic failure (n = 1), and fulminant hepatitis (n = 1) (Table 1).

Table 1 also shows the complications encountered in the 2 groups. The main complications encountered in the CG were HCC recurrence (34.8%) and biliary complications (15.2%), including stones in the common bile duct, bile leakage, bile abscess, intrahepatic and anastomotic strictures, and cholangitis, whereas those in the TG were biliary complications (23.4%), acute rejection (13.1%), and psychosocial problems (10.3%), including excessive alcohol consumption after transplantation, poor drug compliance, and suicide. The rate of HCC recurrence was significantly higher in the CG than in the TG (34.8% *vs*. 4.7%, $P < 0.001$), whereas that of psychosocial problems was significantly higher in the TG than in the CG (10.3% *vs*. 2.2%, $P = 0.023$). Five in 14 patients (36%) with biliary complications in the CG had intrahepatic strictures, some of which were severe and multiple. No patient in the TG developed intrahepatic strictures, and 72% (18/25) biliary complications in this group were attributed to anastomotic strictures, most of which were managed successfully by endoscopic retrograde cholangiographic stenting.

All patients developed only grade III or IV (Classification of surgical complications[4]) complications. These included stroke (n = 1), hemophagocytosis (n = 1), and colon injury during the transplantation procedure in China (n = 1), necessitating colostomy that was performed in China and closed at the TSGH. The diagnosis of acute rejection was confirmed by liver biopsy. Post-transplant *de novo* malignancies included lymphoma (n = 1), gastrointestinal stromal tumor (n = 1), rectal carcinoma (n = 1), lung sarcoma (n = 1), esophageal carcinoma (n = 1), pancreatic carcinoma (n = 1), and mesothelioma (n = 1). Renal complications included acute and chronic renal failure, the need for hemodialysis after transplantation, and complications associated with concurrent kidney transplantation. The survival rate was significantly higher in the TG than in the CG, with the former group exhibiting a trend of greater mean survival duration (Table 1).

HCC recurrence was the major cause of death in the CG, and 87.5% patients in this group had tumors beyond the Milan criteria before transplantation.

Risk factors for survival

Table 2 presents the results of univariate analysis of patient characteristics according to survival. Eight pa-

Table 2 Patient characteristics according to survival

	Survivors (n = 138)	Nonsurvivors (n = 61)	*P*
Donor characteristics			<0.001
China group	47 (34.1%)	45 (73.8%)	
Taiwan group	91 (65.9%)	16 (26.2%)	
Recipient characteristics			
Age	52.3±10.1	51.3±9.8	0.83
F/M	28/110	11/50	0.86
Etiology			
HBV	93	45	0.75
HCV	34	10	0.54
Alcoholic	17	9	0.32
Other	6	0	0.54
HCC	62	47	<0.0001
HCC criteria			
Milan criteria (fit/nonfit)	40/22	11/36	<0.0001
UCSF criteria (fit/nonfit)	44/18	14/33	<0.0001
Complications			
Biliary complications	29	10	0.72
Surgical complications	14	7	0.43
TB infection	5	1	0.37
Renal complications	9	3	0.76
Vascular complications	0	3	0.001
Graft failure	1	8	0.002
Psychosocial problems	4	9	0.002
Acute rejection	21	6	0.099
De novo malignancy	0	7	0.009
Re-exp lap	18	7	0.82
HCC recurrence	2	35	<0.0001

HBV, hepatitis B virus infection; HCV, hepatitis C virus infection; alcoholic, alcoholic-related liver cirrhosis; other, except virus or alcoholic-related liver cirrhosis and HCC; HCC, hepatocellular carcinoma; TB, tuberculosis; re-exp lap, second exploratory laparotomy after liver transplantation; UCSF, University of California, San Francisco.

rameters were found to differ significantly between survivors and nonsurvivors: country (China or Taiwan; $P < 0.001$), Milan criteria status ($P < 0.0001$), UCSF criteria status ($P < 0.0001$), HCC recurrence ($P < 0.0001$), post-transplant de novo malignancy ($P = 0.009$), graft failure ($P = 0.002$), psychosocial problems ($P = 0.002$), and vascular complications ($P = 0.001$). Multivariate analysis identified psychosocial problems, post-transplant *de novo* malignancy, HCC recurrence, and graft failure as independent risk factors for survival (Table 3).

Table 3 Cox Regression Analyses according to Mortality Factors

	Hazard ratio	95% CI	*P*
Group	1.292	0.517–3.230	0.584
Fit Milan criteria	0.898	0.225–3.595	0.880
Fit UCSF criteria	0.530	0.153–1.836	0.317
Vascular complications	1.990	0.583–6.786	0.272
Psychosocial problems	46.304	7.888–271.828	<0.001
De novo malignancy	10.861	1.949–60.520	0.007
HCC recurrence	11.170	4.606–27.092	<0.001
Graft failure	15.379	1.699–139.231	0.015

CI, confidence interval; HCC, hepatocellular carcinoma; UCSF, University of California, San Francisco.

Table 4 Comparison of tumor recurrence rates between HCC patients fitting or not fitting the Milan/UCSF criteria

	Recurrence	Nonrecurrence	*P*
Milan criteria (fit/nonfit)	7/30	44/28	<0.001
UCSF criteria (fit/nonfit)	9/28	49/23	<0.001

Overall survival

The overall survival rate was significantly higher in the TG than in the CG ($P = 0.008$; Fig. 2A). However, this rate did not differ significantly between the 2 groups after adjusting for independent risk factors ($P = 0.58$; Fig. 2B).

Overview of the waiting list at the TSGH

During the study period, 311 patients were on the waiting list at the TSGH. Two patients with acute hepatitis improved after medical treatments and 64 dropped out because of death (n = 44) or extrahepatic HCC metastases (n = 20). The drop-out rate in the TG was 20.6%. The mean waiting time for DDLTs (n = 42) at the TSGH was approximately 6.4 months (Fig. 3).

Tumor recurrence rates among the HCC patients

Subgroup analysis for the HCC patients in our study revealed that the recurrence rate was significantly higher in patients with tumors beyond the Milan criteria or the UCSF criteria than in patients with tumors within these criteria ($P < 0.001$ for Milan and UCSF criteria; Table 4). The recurrence rate was significantly higher in HCC patients in the CG than in those in the TG ($P = 0.005$; Fig. 4).

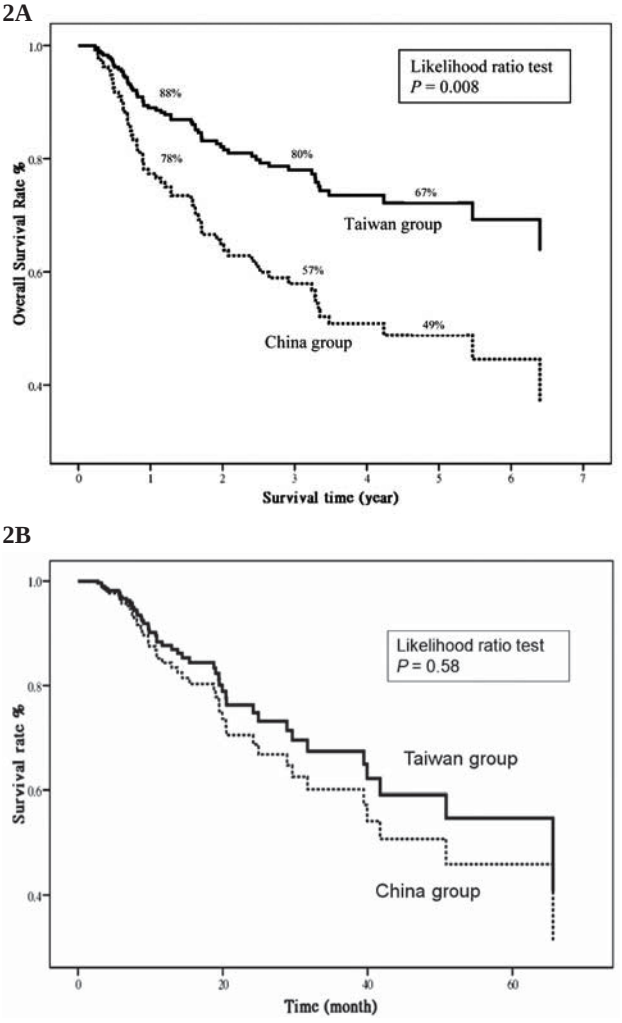

Fig. 2 (A) Comparison of overall survival between the Taiwan group and China group ($P = 0.008$) on the basis of unadjusted data. (B) Survival in the Taiwan group and China group after adjusting for confounding risk factors ($P = 0.58$) .

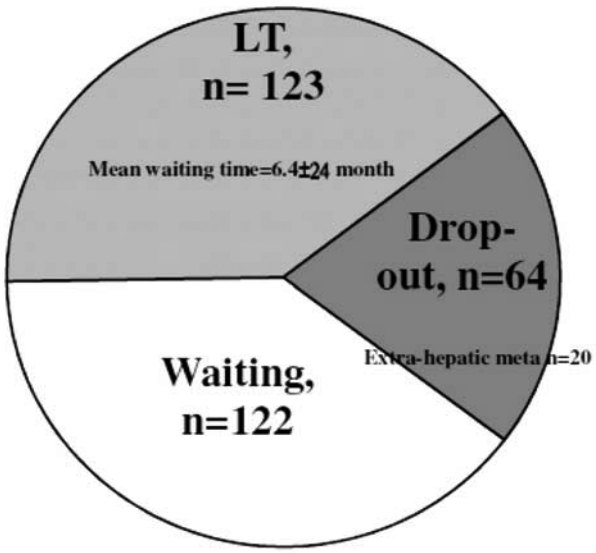

Fig. 3 Distribution of patients on the waiting list at the TSGH (n = 309). Two patients with acute hepatitis who improved after medical treatments are not shown. Drop-out: drop-out from waiting list because of death or extrahepatic metastases, LT: liver transplantation, waiting: still active on the waiting list.

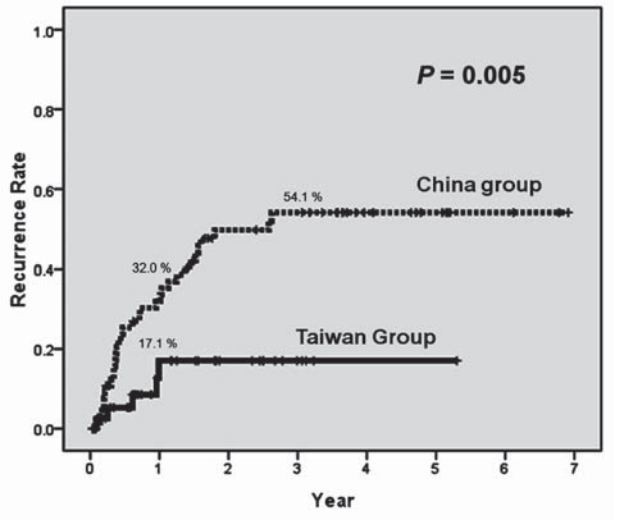

Fig. 4 Prevalence of tumor recurrence among the HCC patients in the Taiwan group and China group
HCC: hepatocellular carcinoma

DISCUSSION

The decrease in the number of patients who received a liver transplant in China and were followed up at the TSGH may reflect the strict regulatory control over the use of human organs in China, which was initiated in 2007.[3]

In this study, the CG patients tended to be from a slightly higher socioeconomic class, and fewer patients in this group reported alcoholism, thus explaining the significantly lower number of patients with alcoholic liver disease (6.5% *vs*. 16.8%, $P = 0.04$) and psychosocial problems after transplantation (2.2% *vs*. 10.3%, $P = 0.023$) in the CG compared with that in the TG.

The 1-year survival rate in the CG was 78%, which is within the range of survival that was recently reported in association with a series of transplants donated after cardiac death (62.5%-86.5%).[5-9] The vascular and bil-

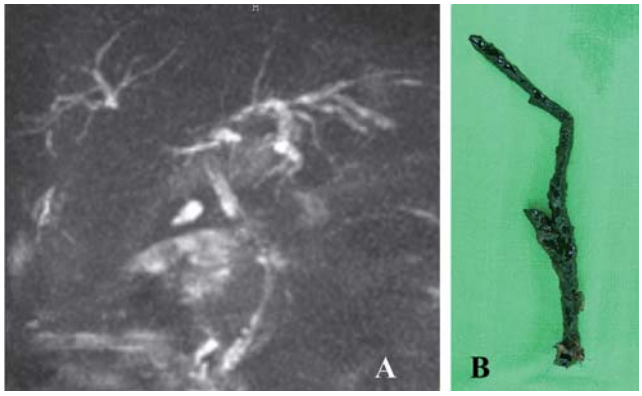

Fig. 5 Formation of intrahepatic duct casts induced by damage to the epithelium of the bile duct
(A) Magnetic resonance cholangiopancreatography showing multiple intrahepatic biliary duct strictures. (B) After exploration, the intrahepatic duct cast was found.

iary complication rates were also comparable between both groups. Although the 5-year survival and vascular complication rates in the present study were similar to a recent report on liver transplantation using livers donated after cardiac death[10] (49% and 2.2% *vs*. 49% and 3.6%, respectively), the biliary complication rate in the present study was lower than that in the previous study (15.2% *vs*. 41.7%).

After liver transplantation, ischemia–reperfusion injury is one of the most important causes of severe damage to the intrahepatic biliary tract, although other etiologies, including chronic ductopenic rejection, liver transplantation across the ABO barrier, and preservation injury are also recognized.[10] Reports have suggested an increase in the rate of biliary complications, mainly intrahepatic ischemic-type biliary strictures, after transplantation using livers donated after cardiac death.[6-10] The biliary complication rate in the CG and TG in our study was within the reported biliary complication rate (5.8%-30%), depending on the types of graft, donor, and biliary anastomosis.[11-16] However, the high incidence of intrahepatic strictures in the CG is a concerning issue because these patients require repeated percutaneous transhepatic cholangiodrainage (PTCD), which influences the daily activities after transplantation and, subsequently, quality of life (QoL). Five patients in the CG developed ischemic biliary complications (5.4%), of which 2 received a second liver transplant and survived, 1 received hepatojejunostomy because of repeated cholangitis and survived, 1 received PTCD drainage, and 1 died of sepsis approximately 20 months after transplantation. Figure 5 shows a patient with multiple intrahepatic bile duct strictures and cast formation who eventually received a second liver transplant. A high incidence of intrahepatic biliary strictures was also reported in a similar study from Hong Kong, in which the incidence of abnormal liver biochemistry and graft failure was higher while the survival rate was lower after transplantation in patients who received a transplant in China than in their counterparts who received a transplant in Hong Kong.[3] In the present study, 3 of 5 patients with ischemic biliary complications developed graft failure, but this biliary complication did not significantly correlate with mortality. Obvious ischemic biliary complications were not observed in the TG, indicating that donation before cardiac death may help in diminishing the severity of ischemic complications.

The HCC recurrence rate was significantly higher in the CG than in the TG in the present study. A likely reason for this is the higher number of patients with HCC beyond the Milan and UCSF criteria in the CG. Subsequently, a higher number of recipients died of HCC recurrence in the CG group (50% *vs*. 6.8%). Since a study at the TSGH in 2006 showed a survival benefit of adjuvant chemotherapy in patients with HCC beyond the Milan criteria[17], most patients with pathologically confirmed HCC beyond the Milan criteria are routinely administered adjuvant chemotherapy (gemcitabine and cisplatin). Since 2006, most patients in the TG with HCC beyond the Milan criteria received adjuvant chemotherapy, decreasing mortality from HCC recurrence. Only a few patients in the CG received adjuvant chemotherapy because the number of patients in that group decreased appreciably since 2006. With regard to survival, although the overall survival rate was significantly higher in the TG than in the CG in this study, the difference became insignificant after adjusting for the risk factors for survival. Nevertheless, according to this observation, patients with advanced HCC should not directly undergo liver transplantation because of the significantly higher risk of HCC recurrence and consequent poor outcome. Instead, alternative treatments should be tried first. Some patients may have a better chance of good outcomes after bridging or downstaging therapies[18,19] such as transarterial chemoembolization, radiofrequency ablation, and cyberknife radiotherapy.

Psychosocial comorbidities can diminish the recipient ability to adapt to the transplant regimen and services. Pretransplant psychosocial assessment of recipients using a multidisciplinary team is warranted. Currently, there is no gold standard for the criteria for psychosocial selection.[20] Some transplantation-specific rating

scales[21,22] have been created to aid in the understanding of psychosocial factors, but studies to determine whether these scales predict a worse outcome after transplantation are lacking. In the TG, a psychiatrist, social worker, and transplant coordinator assessed transplant candidates during the evaluation process. The items in this psychological and mental evaluation form included past psychological disease (including dependence on alcohol and/or drugs), psychological status examinations, and capacity for providing informed consent. The social worker assessed the recipient's: family structure, socioeconomic status and support system, recognition and response to his/her disease, expectation and response to organ transplantatio, decision-making processes, support system during postoperative care. All patients passed the psychosocial evaluation before transplantation; if the patients were in a critical condition and could not communicate well, their closest first-degree relatives were interviewed. The psychosocial comorbidities found in the TG were excessive alcohol consumption after transplantation (n = 5), poor drug compliance (n = 5), and suicide (n = 1). Eight of the 11 patients with psychosocial comorbidities in this group had underlying alcohol-related liver disease. Some patients had mixed etiologies, including viral hepatitis and alcoholic liver disease; therefore, the impact of excessive alcohol consumption could not be accurately determined. However, the long-term effects of excessive alcohol consumption could have contributed to the development of these psychosocial comorbidities, which were found to be independent risk factors for survival in the present study. The criteria used to select patients with alcohol-related liver disease included duration of abstinence >6 months, presence of family or social support, absence of substance or medication abuse, absence of other psychiatric disorders, compliance with recommendations from the treatment team. Some studies have stated that the 6-month abstinence rule is not helpful in predicting post-transplant relapse;[23,24] however, we think that it determines the social and family support the patient can obtain. Regular involvement of an ongoing addiction self-help group and monitoring for relapse during the waiting period by addiction professionals are our goals to decrease the chances of relapse.

An increased incidence of post-transplant malignancies has been reported[25,26], and they are also a major cause of late death in liver transplant recipients.[25,27] Skin cancer and post-transplant lymphoproliferative disease comprise the most common malignancies after liver transplantation, followed by other solid-organ cancers involving the colorectal, esophageal, lung, and genitourinary systems.[28] Risk factors for the development of post-transplant de novo malignancies are thought to be alcoholic liver disease, increasing age, and, possibly, the extent of immunosuppression.[26] Treatment approaches and preventive measures for de novo malignancies vary depending on the type of malignancy.

In conclusion, the overall survival rate was not significantly different between the CG and TG after adjusting for independent risk factors in the multivariate analysis. The post-transplant complication rate was also similar between groups. The rate of HCC recurrence and incidence of intrahepatic biliary strictures were significantly higher in the CG than in the TG, which exhibited a significantly higher incidence of psychosocial problems. The results of the present study suggest that liver transplantation using livers donated after cardiac death can yield comparable outcomes in terms of survival and post-transplant complications. However, patients in the present study who received livers donated after cardiac death tended to exhibit a higher incidence of intrahepatic biliary strictures, resulting in a worse QoL after transplantation. Therefore, patients with advanced HCC should seek expert opinions and receive appropriate tumor treatments until his/her HCC status meets certain widely accepted transplant criteria. An ill-judged decision for liver transplantation without an appropriate indication yields a poor prognosis.

ACKNOWLEDGEMENTS

This study was supported by a grant from the Research & Development Fund of Tri-Service General Hospital (TSGH-C101-022), Taipei, Taiwan.

DISCLOSURE

The authors have no conflicts of interest to declare.

AUTHOR CONTRIBUTIONS

Chen TW and Hsieh CB designed the research and analyzed the data; Chen TW, Chu HC, Liao GS and Chan DC gathered information and undertook the research; Yu CY interpreted the radiological images; Chen TW: drafted and revised the manuscript.

REFERENCES

1. Ravaioli M, Ercolani G, Cescon M, Vetrone G, Voci C, Grigioni WF, D'Errico A, Ballardini G, Cavallari

A, Grazi GL. Liver transplantation for hepatocellular carcinoma: Further consideration on selection criteria. Liver Transpl 2004;10:1195-1202, doi: 10.1002/lt.20239.
2. Ringe B, Strong RW. The dilemma of living liver donor death: to report or not to report? Transplantation 2008;85:790-793, doi: 10.1097/TP.0b013e318167345e.
3. Fan ST, Wang H, Lam BK. Follow-up of Chinese liver transplant recipients in Hong Kong. Liver Transpl 2009;15:544-550, doi: 10.1002/lt.21720.
4. Dindo D, Demartines N, Clavien PM. Classification of surgical complications. A new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 2004;240:205-213.
5. Muiesan P, Girlanda R, Jassem W, Melendez HV, O'Grady J, Bowles M, Rela M, Heaton N. Single-center experience with liver transplantation from controlled non-heart beating donors: a viable source of grafts. Ann Surg 2005;242:732-738.
6. Abt P, Crawford M, Desai N, Markmann J, Olthoff K, Shaked A. Liver transplantation from controlled non-heart beating donors: an increase incidence of biliary complications. Transplantation 2003;75:1659-1663.
7. Fukumori T, Kato T, Levi D, Olson L, Nishida S, Ganz S, Nakamura N, Madariaga J, Ohkohchi N, Satomi S, Miller J, Tzakis A. Use of older controlled non-heart-beating donors for liver transplantation. Transplantation 2003;75:1171-1174.
8. D'Alessandro AM, Hoffmann RM, Knechtle SJ, Odorico JS, Becker YT, Musat A, Pirsch JD, Sollinger HW, Kalayoglu M. Liver transplantation from controlled non heart-beating donors. Surgery 2000;128:579-588.
9. Monbaliu D, Van Gelder F, Troisi R, de Hemptinne B, Lerut J, Reding R, de Ville de Goyet J, Detry O, De Roover A, Honore P, Donckier V, Gelin M, Ysebaert D, Aerts R, Coosemans W, Pirenne J. Liver transplantation using non heart-beating donors: Belgian experience. Transplant Proc 2007;39:1481-1484.
10. Suarez F, Otero A, Solla M, Arnal F, Lorenzo MJ, Marini M, Vázquez-Iglesias JL, Gómez M. Biliary complications after liver transplantation from Maastricht category-2 non-heart beating donors. Transplantation 2008;85:9-14, doi: 10.1097/01.tp.0000297945.83430.ce.
11. Sawyer RG, Punch JD. Incidence and management of biliary complications after 291 liver transplants following the introduction of transcystic stenting. Transplantation 1998;66:1201-1207.
12. Hernandez Q, Ramirez P, Munitiz V, Piñero A, Robles R, Sanchez-Bueno F, Rodriguez JM, Lujan J, Acosta F, Miras M, Pons JA, Parrilla P. Incidence and management of biliary tract complications following 300 consecutive orthotopic liver transplants. Transplant Proc 1999;31:2407-2408.
13. Rerknimitr R, Sherman S, Fogel EL, Kalayci C, Lumeng L, Chalasani N, Kwo P, Lehman GA. Biliary tract complications after orthotopic liver transplantation with choledo-chocholedochostomy anastomosis: endoscopic findings and results of therapy. Gastrointest Endosc 2002;55:224-231.
14 Park JS, Kim MH, Lee SK, Seo DW, Lee SS, Han J, Min YI, Hwang S, Park KM, Lee YJ, Lee SG, Sung KB. Efficacy of endoscopic and percutaneous treatments for biliary complications after cadaveric and living donor liver transplantation. Gastrointest Endosc 2003;57:78-85.
15. Qian YB, Liu CL, Lo CM, Fan ST. Risk factors for biliary complications after liver transplantation. Arch Surg 2004;139:1101-1105.
16. Thethy S, Thomson BN, Pleass H, Wigmore SJ, Madhavan K, Akyol M, Forsythe JL, James Garden O. Management of biliary tract complications after orthotopic liver transplantation Clin Transplant 2004;18:647-653.
17. Hsieh CB, Chou SJ, Shih ML, Chu HC, Chu CH, Yu JC, Yao NS. Preliminary experience with gemcitabine and cisplatin adjuvant chemotherapy after liver transplantation for hepatocellular carcinoma. European Journal of Surgical Oncology (EJSO) 2008;34:906-910, doi: 10.1016/j.ejso.2007.11.014.
18. Ravaioli M, Grazi GL, Piscaglia F, Trevisani F, Cescon M, Ercolani G, Vivarelli M, Golfieri R, D'Errico Grigioni A, Panzini I, Morelli C, Bernardi M, Bolondi L, Pinna AD. Liver transplantation for hepatocellular carcinoma: results of down-staging in patients initially outside the Milan selection criteria. Am J Transplant 2008;2547-2557, doi: 10.1111/j.1600-6143.2008.02409.x.
19. De Luna W, Sze DY, Ahmed A, Ha BY, Ayoub W, Keeffe EB, Cooper A, Esquivel C, Nguyen MH. Transarterial chemoinfusion for hepatocellular carcinoma as downstaging therapy and a bridge toward liver transplantation. Am J Transplant 2009;9:1158-1168, doi: 10.1111/j.1600-6143.2009.02576.x.
20. Levenson J, Olbrisch M: Psychosocial evaluation of organ transplant candidates. A comparative survey of process, criteria, and outcomes in heart, liver, and kidney transplantation. Psychosomatics 1993;34:314-323.

21. Twillman R, Manetto C, Wellisch DK, Wolcott DL. The Transplant Evaluation Rating Scale. A revision of the psychosocial levels system for evaluating organ transplant candidates. Psychosomatics 1993;34:144-153.
22. Olbrisch M, Levenson J, Hamer R: The PACT: A rating scale for the study of clinical decision-making in psychosocial screening of organ transolant candidates. Clin Transplant 1989;3:164-169.
23. Yates W, Martin M, LaBrecque D, Hillebrand D, Voigt M, Pfab D. A model to examine the validity of the 6-month abstinence criterion for liver transplantation. Alcohol Clin Exp Res 1998;22:513-517.
24. Platz K, Mueller A, Spree E, Schumacher G, Nüssler NC, Rayes N, Glanemann M, Bechstein WO, Neuhaus P. Liver transplantation for alcoholic cirrhosis. Transpl Int 2000;13:S127-S130.
25. Saigal S, Norris S, Muiesan P, Rela M, Heaton N, O'Grady J. Evidence of differential risk for posttransplantation malignancy based on pretransplantation cause in patients undergoing liver transplantation. Liver Transpl 2002;8:482-487.
26. Jain A, DiMartini A, Kashyap R, Youk A, Rohal S, Fung J. Long-term follow-up after liver transplantation for alcoholic liver disease under tacrolimus. Transplantation 2000;70:1335-1342.
27. Sheiner PA, Magliocca JF, Bodian CA, Kim-Schluger L, Altaca G, Guarrera JV, Emre S, Fishbein TM, Guy SR, Schwartz ME, Miller CM. Long-term medical complications in patients surviving ≥ 5 years after liver transplant. Transplantation 2000;69:781-789.
28. Watt KD , Pedersen RA, Kremers WK, Heimbach JK, Sanchez W, Gores GJ. Long-term probability of and mortality from de novo malignancy after liver transplantation. Gastroenterology 2009;137:2010-2017, doi: 10.1053/j.gastro.2009.08.070.