Cadaveric liver transplant from older donors

Hanan M. Alghamdi, MD, FICS, *Michael D. Crawford,* MBBS, FRACS, *James P. Gallagher,* MBBS, FRACS, *Geoff W. Mccaughan,* PD, FRACP, *Simone I. Strasser,* MD, FRACP, *Deborah J. Verran,* MBChB, FRACS.

ABSTRACT

الهدف: ننشر هنا نتيجة خبرتنا الحديثه في مجال زراعه الكبد من متبرع ميت دماغيا كبير في السن (اكبر من 60 عاما)(م. ك.) و مقارنتها بالمتبرع الصغير (اصغر من 60 عاما)(م. ص.).

الطريقه: جمعت البيانات المحفوظة بطريقه مستقبليه من ملفات المرضى و من قاعدة المعلومات. ما بين أول عام 1997م و آخر عام 2004م كان هناك 313 عملية زراعة كبد أدخلت في البحث، منها 51 (16%) من متبرعين كبار.

النتائج: في هذا البحث (هناك 313 عمليه زراعة كبد) وجد هناك نسبه أكبر من المتلقين لكبد من(م. ك.) يحملون فصيلة دم O:51% مقابل 33% مقارنه ب (م. ص.) (p= 0.025) و أيضا فشل كبدي حادي: 9.8% مقابل 5% (p=0.018). من ناحية أخرى، لم يوجد أي اختلاف بين مجموعة (م. ك.) و (م. ص.) من حيث عمل الكبد الضعيف الأولي: 16/51 (31%) مقابل74/262 (28%) أو فشل الكبد النهائي: 6.5% مقابل 6.5% أو في فقد الكبد كاملا15/51 : (29%) مقابل 62/262 (24%)أو نسبت التدهن في الكبد: (35%)14/40 مقابل 82/232 (36%) أو في تخثر الشريان الكبدي (2%)1/51 مقابل (3%)8/262 أو في بقاء الكبد على مدى عام: 82% مقابل 87% أو على مدى ثلاثة أعوام 75% مقابل 81% أو على مدى خمسه أعوام 75% مقابل 77% (p = 0.27 log rank) أو في مدى بقاء المتلقي للكبد على مدى عام: 86% مقابل 89% أو على مدى ثلاثة أعوام: 79% مقابل 83% أو على مدى خمسه أعوام: 79% مقابل 80% (p = 0.336 log rank).

خاتمة: يمكن لنا أن نقوم بزراعه كبد من متبرع كبير في السن و بنتائج مقبولة تحت ضوابط تشرح في داخل البحث.

Objective: To examine the effects of cadaveric donor age on outcomes following orthotopic liver transplantation (OLT).

Methods: Data were collected on all patients who underwent OLT between January 1997 and December 2004 at the Royal Prince Alfred Hospital, Sydney, New South Wales, Australia. During this period, 313 OLTs were performed: 51 patients (16%) received older donor livers (OD; 60 or more years old), and 262 (84%) received younger donor livers (YD; less than 60 years old).

Results: In the study group (313 patients), we found significantly more recipients of OD liver with blood group O:51% versus 33% (p=0.025) and with fulminant hepatic failure: 9.8% versus 5% (p=0.018) compared to YD recipients. No difference between OD and YD liver recipients was found in initial poor graft function: 16/51 (31%) versus 74/262 (28%), primary non-functioning: 6.5% versus 6.5%, the overall graft loss: 15/51 (29%) versus 62/262 (24%), post-revascularization liver biopsy steatosis: 14/40 (35%) versus 82/232 (36%) or hepatic artery thrombosis: 1/51 (2%) versus 8/262 (3%). There was no difference in graft actuarial survival between OD and YD recipients at 1, 3, and 5 years, 82% versus 87%, 75% versus 81%, and 75% versus 77% (p=0.27 log rank) or patient actuarial survival, 86% versus 89%, 79% versus 83%, and 79% versus 80% (p=0.336 log rank).

Conclusion: Orthotopic liver transplantation can be achieved with acceptable outcomes using selected livers from older deceased donors.

Saudi Med J 2008; Vol. 29 (4): 533-538

From the Australian National Liver Transplant Unit (Alghamdi, Crawford, Gallagher, Mccaughan, Strasser, Verran), Royal Prince Alfred Hospital, Camperdown/Sydney, New South Wales, Australia, Department of General Surgery, Division of Hepatobiliary Surgery, (Alghamdi), Vancouver General Hospital, University of British Columbia, Vancouver, Canada, Department of Surgery, (Alghamdi), King Fahad University Hospital and King Faisal University, Kingdom of Saudi Arabia.

Received 21st July 2007. Accepted 27th January 2008.

Address correspondence and reprint request to: Dr. Hanan M. Alghamdi, Department of Surgery, Division of Hepatobiliary Surgery, 910 West 10th Avenue, Room # 3100, Vancouver, BC, Canada V5Z 4E3. Tel. +1 (604) 783-7347, Fax. +1 (604) 875-5869. E-mail: hananghamdi@yahoo.com

Disclosure. All authors declare no conflict of interest with these products.

Donor organs available for transplantation remain in short supply relative to demand. In recent years, many transplant centers have expanded their selection criteria to consider orthotopic liver transplantation (OLT) of organs from donors who were previously considered marginal. These expanded donor selection criteria now may include older donors.[1-4] Initial case reports of successful OLT from deceased older donors (OD), 60 years of age, or older at time of death, have challenged the traditional view of donors considered marginal due to advanced age, and have encouraged wider acceptance. At the Australian National Liver Transplant Unit of the Royal Prince Alfred Hospital, Camperdown, New South Wales, Australia, we accepted the first OD liver for OLT in 1991 as an urgent case. Over the years, there has been a gradual increase in the number of OD liver transplants at our institution, and the age limit has been extended up to 60 years of age.[5] We report here our recent experience with OLT using OD livers compared with younger donor (YD, less than 60 years old) livers, in terms of outcome.

Methods. Between January 1997 and December 2004, 344 OLT were performed at the Australian National Liver Transplant Unit, Royal Prince Alfred Hospital, Sydney, New South Wales, Australia. Of those, 31 had either undergone previous liver transplantation or were under the age of 18, and were therefore excluded. The remaining 313 cases were primary OLT performed on adult recipients from brain-dead cadaveric donors. Of these, 51 (16%) were OD livers while 262 (84%) were YD livers. All data were retrieved from patient charts and hospital electronic databases (prospectively maintained).

Donor data. Donor information collected included age, gender, and cause of death. The decision for accepting a cadaveric organ was based on donor's demographic (for example, weight/height, and blood group), clinical (for example, no hemodynamic instability, and the presence of functioning organs), biochemical parameters of the organ donor (for example, normal liver function test, renal function test, electrolyte, and viral screening) and anatomical criteria, regardless of age. The decision to use the liver was the responsibility of the transplanting surgeon. Livers that appear grossly normal (more strict evaluation for OD livers) were accepted. Pre-implantation biopsy was performed and processed before transplantation only when there was a suspicion. Acceptable liver steatosis was equal to or less than 30%. Organs were retrieved based on the usual standard method, involving an in vivo dissection prior to aortic rapid cold perfusion with 4-5 liters Ross®solution (produced by ORION Laboratories Pty Ltd, 25-29 Delawney St, Balcatta Western Australia 6021) and 2 Liters of UW® (University of Wisconsin) solution. An additional arterial and portal venous flush was performed on the back table with 2 liters of UW solution.[6] All authors declare no conflict of interest with these products.

Recipient data. Data obtained included recipient demographics (age, gender, blood group, indication for OLT), causes of graft loss and requirement for re-transplantation. Recipient severity status at time of OLT was according to the United Network for Organ Sharing (UNOS).[7] Complete data on postperfusion protocol liver biopsies were found in 40 of the OD recipients, and 232 of YD recipients. The degree of steatosis was objectively categorized by an experienced pathologists using the following standardized grades: Grade 0, 0-4% macrovesicular steatosis, grade I (mild), 5-15% macrovesicular steatosis; grade II (moderate), 16-30% macrovesicular steatosis, and grade III (severe), 31-45% macrovesicular steatosis.[8] Initial poor graft function (IPGF) is defined as serum aspartate aminotransferase and/or alanine aminotransferase level equal to or more than 1500 U/ mL on 2 consecutive measurements within the first 72 hours post transplant. Primary non-functioning (PNF) is defined as poor function of the allograft leading to death of the recipient or retransplantation within 7 days.[9] All patients were commenced on combined immunosuppression according to the local protocols consisting of calcineurin inhibitors-based regimen and steroids with or without mycophenolate mofetil. Antibiotic and antiviral prophylaxis were administered perioperatively and modified according to the clinical situation. All patients were followed for at least another year. Graft and patient survival at 1, 3, and 5 years were calculated.[10]

Comparisons between OD and YD liver recipients were performed using Student's t-test for independent parametric variables, and the chi-square test for dichotomous variables. Pair wise comparisons were performed using the z-test of relative proportions. Patient and graft survival were compared using the log rank test. Differences were considered significant at $p<0.05$. Graft and patient actuarial survival curves were calculated using the Kaplan-Meier method. All analysis were carried out using Statistical Package for Social Sciences and Sigmastat.

Results. ***Donors.*** In the study period, there was a total of 313 OLT performed, 51 with OD livers, and 262 with YD livers. There were significant differences in donor cause of death between the OD and YD groups. Within the OD group, the leading cause of death was intracerebral hemorrhage (ICH), it accounted for 40 of 51 OD deaths (78%) versus 127 of 262 YD deaths (48%) ($p=0.0001$). Conversely, motor vehicle accidents (MVAs) accounted for none of the OD deaths versus 53 (20%) of YD deaths ($p=0.0001$) (**Table 1**).[11,12]

Recipient data. The distribution among OD versus YD recipients of age, gender, blood group, UNOS Severity Status, and indications for transplantation are summarized in **Table 2.** No significant differences were seen in the recipient's mean age at time of transplant between the OD (51 ± 9.9 years) and YD (49 ± 10.5 years) groups (p=0.082). All OD liver recipients except one, underwent whole-liver transplantation to avoid the confounding factor of split-liver transplantation in the face of a potentially marginal older organ. A significant number of OD liver recipients had blood group O, 51% versus 33% compared to YD group (p=0.025). Although there were more patients in status 4 in the OD group compared to YD group (8% versus 4%), the difference was not significant (p=0.258), however, more patients with fulminant hepatic failure (FHF), 5 (9.8%) received liver from OD versus 13 (5%) from YD (p=0.018). Nevertheless, chronic active hepatitis (CAH) remains the most common indication for OLT in both groups. The distribution of OD and YD recipients by steatosis grade (post-revascularization liver biopsy) is presented in **Table 3**. Analysis of the relative distribution by steatosis grade of OD versus YD recipients revealed no significant overall difference (p=0.855). Similarly, comparisons between OD versus YD recipients for each steatosis grade revealed no significant differences. Likewise, comparison of the incidence of IPGF among OD versus YD recipients (31.4% versus 28.2%) revealed no significant difference (p=0.778). There was one case (6.5%) of PNF in the OD group versus 3 (6.5%) in the YD group, while the overall graft loss was seen in 15/51 (29%) versus 62/262 (24%). Re-transplant was required in 2 of the OD recipients versus 7 of the YD recipients (**Table 4**). It was undoubtedly, a comparable graft actuarial survival in OD and YD recipients at 1, 3, and 5 years, 82% versus 87%, 75% versus 81% and 75% versus 77% (p=0.27 log rank) (**Figure 1**). The most common cause of graft loss was patient death in

Table 1 - Donors characteristics.

Variable	OD (n=51)	YD (n=262)	*P*-value
	n (%)		
Age (years)			
Mean ± SD	66 ± 5	37 ± 14	<0.0001
Range	60 - 78	8 - 59	
Gender			
Male	30 (59)	161 (61.5)	
Female	21 (41)	101 (38.5)	0.755
Cause of death			
ICH	40 (78)	127 (48)	0.0001
MVA	0 (0)	53 (20)	0.0001
Cardiac arrest	1 (2)	6 (2)	0.385
Cerebral tumor	0 (0)	4 (1.5)	0.421
Other head injury	3 (6)	36 (14)	0.109
Other	7 (14)	23 (9)	0.092
Suicide	0 (0)	12 (5)	0.080
Tumor	0 (0)	1 (0.5)	0.598

ICH - intra cranial hemorrhage, MVA - motor vehicle accident, OD - older donor, YD - younger donor

Table 2 - Recipients Data.

Variables	OD (n=51)	YD (n=262)	*P*-value
	n (%)		
Age (years)			0.082
Mean ± SD	51 ± 9.9	49 ± 10.5	
Range	18 - 69	18 - 68	
Gender			0.062
Male	31 (61)	194 (74)	
Female	20 (39)	68 (26)	
Blood groups			0.003
O	26 (51)	87 (33)	0.025
A	19 (37)	120 (46)	0.180
B	4 (8)	44 (17)	0.725
AB	2 (4)	11 (4)	0.548
UNOS Severity Status			0.518
Status 4 (urgent)	4 (8)	10 (4)	0.258
Status 3 (hospitalized)	5 (10)	28 (11)	0.197
Status 2 (frequent hospitalization)	16 (31)	71 (27)	0.095
Status 1 (outpatient)	26 (51)	153 (58)	0.258
Types of transplant			0.243
Whole organ	50 (98)	239 (91)	0.429
Split liver	1 (2)	23 (9)	0.318
Indications for OLT			0.018
CAH	16 (31.4)	97 (37)	0.587
Alcoholic cirrhosis	10 (19.6)	30 (11.5)	0.254
CC	5 (9.8)	6 (2.3)	0.024
HCC	6 (11.8)	30 (11.5)	0.584
Metabolic	1 (2)	23 (8.8)	0.659
FHF	5 (9.8)	13 (5)	0.243
PBC	4 (7.8)	12 (4.6)	0.367
PSC	1 (2)	31 (11.8)	0.550
BA	1 (2)	2 (0.7)	0.487
Other	2 (3.8)	18 (6.8)	0.684

CAH - chronic active hepatitis, HCC - hepatocelluar carcinoma, CC - cryptogenic cirrhosis, FHF - fulminant hepatic failure, PBC - primary biliary cirrhosis, PSC - primary schlerosing cholongitis, BA - biliary atresia, OLT - orthotopic liver transplantation, UNOS - United Network for Organ Sharing , OD - older donor, YD - younger donor

Table 3 - Steatosis and initial poor graft function.

Variable	OD (n= 40)	YD (n=232)	*P*-value
	n (%)		
Steatosis			0.855
Grade 0 (None)	26 (65)	150 (64)	0.542
Grade I (Mild)	11 (27)	55 (24)	0.921
Grade II (Moderate)	2 (5)	16 (7)	0.584
Grade III (Severe)	1 (3)	11 (5)	0.498
No data	11/51 (23)	31/262 (12)	
IPGF	16/51 (31)	74/262 (28)	0.400

IPGF - Initial Poor Graft Function, OD - older donor, YD - younger donor

Table 4 - Graft failure and retransplant.

Variable	OD (n= 51)	YD (n=262)	*P*-value
	n (%)		
Graft failure (total)	15 (29)	62 (24)	0.602
Patient death	11 (74)	31 (50)	0.548
Recurrent	1 (6.5)	8 (13)	0.439
HAT	1 (6.5)	8 (13)	0.429
Recurrent HCC	0 (0)	6 (9.5)	0.721
PNF	1 (6.5)	4 (6.5)	0.244
Chronic rejection	1 (6.5)	2 (3)	0.389
Others		3 (5)	0.722
Indications for retrasplant			0.852
PNF	1	3	0.794
HAT	1	3	0.804
Chronic rejection	0	1	0.981

PNF - primary non-functioning, HAT - hepatic artery thrombosis, HCC -hepatocelluar carcinoma, OD - older donor, YD - younger donor

Table 5 - Cause of recipient death.

Variable	OD	YD	*P*-value
	n (%)		
Cause of recipient death	11	54	0.767
Graft failure	3 (27)	15 (27)	0.822
Sepsis	4 (37)	12 (22.5)	0.921
Malignancy developed de novo OLT	2 (18)	4 (7.5)	0.789
Recurrent HCC	0 (0)	6 (11)	0.994
Cardiovascular	0 (0)	5 (9)	0.998
Operative: Hemorrhage	0 (0)	2 (4)	0.980
Respiratory complication	0 (0)	2 (4)	0.910
Cerebrovascular	0 (0)	1 (2)	0.879
GI hemorrhage	0 (0)	1 (2)	0.892
Other	2 (18)	6 (11)	0.587

GI - gastrointestinal, OLT - orthotopic liver transplant

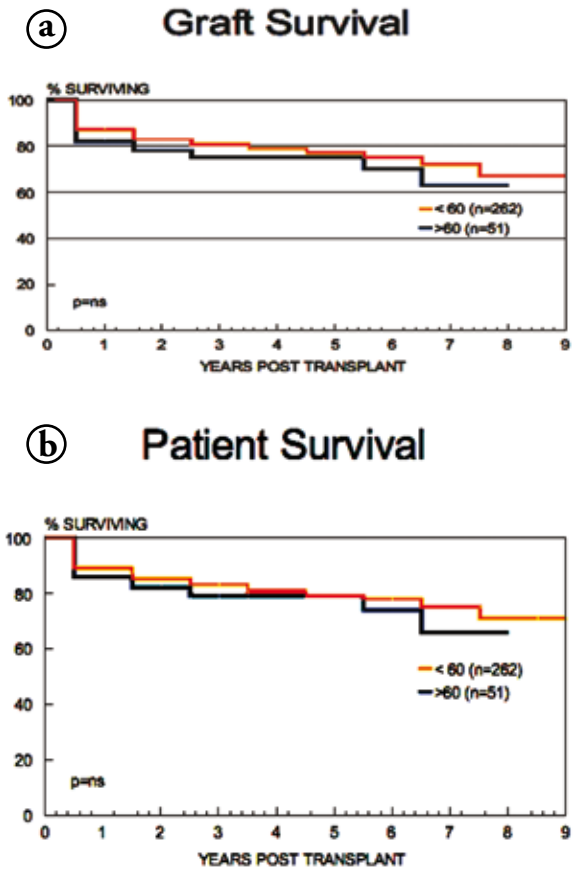

Figure 1 - a) Graft survival (upper panel) and b) patient survival (lower panel) for all recipients in the older and younger donor groups.

both groups. Hepatic artery thrombosis (HAT) was blamed for 1/51 (2%) of OD group graft loss versus 8/262 (3%) of YD group (**Table 4**). In the study period, the total death in the OD group was 11/51 (21%) mostly due to sepsis in 4/11 (37%). While in the YD group there were 54/262 (20.6%) deaths mainly due to graft failure in 15/54 (27%) (**Table 5**). Clearly, there was no significant difference in patient actuarial survival between OD and YD groups at 1, 3, and 5 years, 86% versus 89%, 79% versus 83%, and 79% versus 80% (p=0.336 log rank) (**Figure 1**).

Discussion. Adopting new strategies to increase the donor pool includes live donors, split livers, or livers from marginal donors, for example, older donor, deceased cardiac donor, liver with steatosis, HCV positive donor, and so forth, are ways of expanding the donor criteria.[13] Enthusiasm for using OD livers stems from the initial reported successes in mostly urgent

transplants.[2-4] Over the years, the acceptable donor age has been pushed upwards from age 50 to age 60, and even to age 80 by some centers.[2-4,14-17] The unique ability of the hepatocytes to regenerate and preserve its functional capacity may translate into an organ that is effectively younger than the actual age of the donor. Although several reports warned against an increased incident of HAT in older donors,[18] the impact probably diminished due to the unique dual blood supply to the liver, that exceeds the liver metabolic requirements. Furthermore, some investigators suggest that the liver vessels are less affected by atherosclerosis, especially the parenchymal part, which could be attributed to it's low blood flow pressure, but still the extrahepatic part needs to be inspected.[19] Likewise, bile ducts can also be affected by aging, which needs to be evaluated in the outcome of any transplant study using OD livers.[2,20,21] On the other hand, data concerning the safety, and long-term reliability of extreme OD livers, such as those from donors above the age of 80, are lacking.[12,22] Feng et al[11] showed in a recent multivariant analysis that the affect of age becomes evident only when the donor age is greater than 40, and particularly so over 60 years of age. Cuende et al[23] also reported a significant relative risk of 1.27 on graft survival when donor age is 50-69 years, and a relative risk of 1.4 for 70 years of age.

In this study, ICH was more common in the OD recipient group (78%), while MVA was the most common cause of death in the YD recipient group (**Table 1**). All but one OD livers were transplanted whole to optimize functional capacity, the one exception was a split liver, where the right lobe was successfully transplanted at our Unit. Likewise, low-grade steatosis in OD livers reflects our strict selection criteria, which is also reflected in the low incidence of IPGF.[24]

It is clearly shown in this study that graft survival does not differ significantly between the 2 groups for up to 5 years follow up. Patient death was the most common cause of graft loss in both groups. The HAT was responsible for one graft loss in the OD group (which was successfully retransplanted) compared to 8 in the YD group.[25] Likewise, patient survival was comparable in both groups. Sepsis was the main cause of death in the OD recipient group, while graft failure was the leading cause of death in the YD recipient group.

In our Unit, we try to avoid transplanting HCV-positive recipients with an OD liver. The rationale for this stems from the notorious association between donor age, and the severity of recurrent hepatitis C after OLT, as suggested previously by some authors.[26-30] Nevertheless, this strategy is challenged by pressing situations such as the presence of HCC, which ultimately prioritizes the patient for transplant to avoid exempt by the Milan's criteria. Likewise, advanced stage of liver failure or rare blood groups are other scenarios that press for accepting marginal livers.[31] The cut-off points at which donor age impacts a risk on severe HCV recurrence has not been clearly defined. In this study, we did not focus specifically on this group. The outcome of OD transplantation in HCV positive recipients merits further study. Organ viability criteria include biochemical, morphological, and functional parameters that must be fulfilled by prospective donor organs. These criteria attempt to ensure that transplanted organs function after extraction, transformation, implantation, and reperfusion without transmission of infection or tumor. In recent years, the gross and microscopic appearance has become one of the fundamental criteria for selection of potentially viable organs. At present, there is no age limit for hepatic and renal donation, the principal contraindication is chronic organ damage. Currently, the only absolute exclusion criteria are HIV infection, uncontrolled tumor, and bacterial or viral infections. The use of each organ must be decided on an individual basis, after a detailed analysis of all the viability criteria, and careful weighing of the advantages and disadvantages of the proposed organ for the recipient.[32]

In conclusion, acceptable outcomes can be achieved in OLT using selected livers from older deceased donors. The presences of HCC, guarded clinical status, or rare blood groups are some of the many factors that influence the decision to use organs from older donors.

Acknowledgment. *I would like to acknowledge the work carried out by our data manager Mr. Patrick Tang and Mrs. Pamela Dilworth.*

References

1. Alexander JW, Vaughan WK. The use of "marginal" donors for organ transplantation: The influence of donor age on outcome. ***Transplantation*** 1991; 51: 135-141.
2. Washburn WK, Johnson LB, Lewis WD, Jenlins RL. Graft function and outcome of older (> or = 60 years) donor livers. ***Transplantation*** 1996; 61: 1062-1066.
3. Marino IR, Doyle HR, Doria L, Aldrighetti T, Gayowski C, Scotti-Foglient H, et al. Outcome of liver transplantation using donors 60 to 79 years of age. ***Transplant Proc*** 1995; 27: 1184-1185.
4. Wall WJ, Mimeault R, Grant DR, Bloch M. The use of older donor livers for hepatic transplantation. ***Transplantation*** 1990; 49: 377-381.
5. Verran DJ, Gurkan A, Dilworth P, Painter D, Chui A, Dorney S, et al. Inferior liver allograft survival from cadaveric donors > 50 years of age? ***Clin Transplantation*** 2001; 15: 106-110.
6. Chui AK, Thompson JF, Lam D, Koutalistras N, Wang L, Verran DJ, et al. Cadaveric liver procurement using aortic perfusion only. ***Aust NZ J Surg*** 1998; 68: 275-277.
7. United Network for Organ Sharing. Available from: http://www.unos.org.
8. Chui AK, Shi LW, Rao AR, Verran DJ, Painter D, Koorey D, et al. Donor fatty (steatotic) liver allografts in orthotopic liver transplantation: a revisit. ***Transplant Proc*** 1998; 307: 3286-3287.

9. Nanashima A, Pillay P, Verran DJ, Painter D, Nakasuji M, Crawford M, et al. Analysis of initial poor graft function after orthotopic liver transplantation: experience of an australian single liver transplantation center. ***Transplant Proc*** 2002; 344 :1231-1235.
10. Verran DJ, Asfar SK, Ghent CN, Grant DR, Wall WJ. Biliary reconstruction without T tubes or stents in liver transplantation: report of 502 consecutive cases. ***Liver Transpl Surg*** 1997; 34: 365-3673.
11. Feng S, Goodrich NP, Bragg-Gresham JL, Dykstra DM, Punch JD, DebRoy MA, et al. Characteristics associated with liver graft failure: the concept of a donor risk index. ***Am J Transpl*** 2006; 6: 783-790.
12. Rifai K, Sebagh M, Karam V, Saliba F, Azoulay D, Adam R, et al. Donor age influences 10-year liver graft histology independently of hepatitis C virus infection. ***Hepatology*** 2004; 41: 446-453.
13. Lopez-Navidad A, Caballero F. Extended criteria for organ acceptance. Strategies for achieving organ safety and for increasing organ pool. ***Clin Transplant*** 2003; 17: 308-324.
14. Kim DY, Cauduro SP, Bohorquez HE, Ishitani MB, Nyberg SL, Rosen CB. Routine use of livers from deceased donors older than 70: is it justified? ***Transpl Int*** 2005; 18: 73-77.
15. Cescon M, Grazi GL, Ercolani G, Nardo B, Ravaioli M, Gardini A, Cavallari A. Long-term survival of recipients of liver grafts from donors older than 80 years: is it achievable? ***Liver Transpl*** 2003; 911: 1174-1180.
16. Nardo B, Masetti M, Urbani L, Caraceni P, Montalti R, Filipponi F, et al. Liver transplantation from donors aged 80 years and over: pushing the limit. ***Am J Transplant*** 2004; 4: 1139-1147.
17. Janssen H, Malago M, Erhard J, Lange R, Testa G, Vester U, et al. Donor age in Liver Transplantation: Is There a Limit? ***Transplant Proc*** 2001; 33: 1504.
18. Grazi GL, Cescon M, Ravaioli M, Ercolani G, Pierangeli F, D'Errico A, et al. A revised consideration on the use of very aged donors for liver transplantation. ***Am J Transplant*** 2001; 1: 61-68.
19. Popper H. Aging and the liver. ***Prog Liver Dis*** 1986; 8; 659-683.
20. Yersiz H, Shaked A, Olthoff K, Imagawa D, Shackleton C, Martin P, et al. Correlation between donor age and the pattern of liver graft recovery after transplantation. ***Transplantation*** 1995; 60: 790-794.
21. Borchert D, Glanemann M, Mogl M, Langrehr JM, Neuhaus P. Older liver graft transplantation, cholestasis and synthetic graft function. ***Transpl Int*** 2005; 18: 709-715.
22. Busquets J, Xiol X, Figueras J, Jaurrieta E, Torras J, Ramos E, et al. The impact of donor age on liver transplantation: influence of donor age on early liver function and on subsequent patient and graft survival. ***Transplantation*** 2001; 71: 1765-1771.
23. Cuende N, Miranda B, Canon JF, Garrido G, Matesanz R. Donor characteristics associated with liver graft survival. ***Transplantation*** 2005; 79: 1445-1452.
24. Rull R, Vidal O, Momblan D, González FX, López-Boado MA, Fuster J, et al. Evaluation of potential liver donors: limits imposed by donor variables in liver transplantation. ***Liver Transplant*** 2003; 9: 389-393.
25. Oh CK, Sanfey HA, Pelletier SJ, Sawyer RG, McCullough CS, Pruett TL, et al. Implication of advanced donor age on the outcome of liver transplantation. ***Clin Transplant*** 2000: 14: 386-390.
26. Lake JR, Shorr JS, Steffen BJ, Chu AH, Gordon RD, Wiesner RH, et al. Differential effects of donor age in liver transplant recipients infected with hepatitis B, hepatitis C and without viral hepatitis. ***Am J Transpl*** 2005; 5: 549-557.
27. Berenguer M, Prieto M, San Juan F, Rayón JM, Martinez F, Carrasco D, et al. Contribution of donor age to the recent decrease in patient survival among HCV-infected liver transplant recipients. ***Hepatology*** 2002; 36: 202-210.
28. Machicao VI, Bonatti H, Krishna M, Aqel BA, Lukens FJ, Nguyen JH, et al. Donor age affects fibrosis progression and graft survival after liver transplantation for hepatitis C. ***Transplantation*** 2004; 77: 84-92.
29. Russo MW, Galanko JA, Zacks SL, Beavers KL, Fried MW, Shrestha R, et al. Impact of donor age and year of transplant on graft survival in liver transplant recipients with chronic hepatitis C. ***Am J Transpl*** 2004; 4: 1133-1138.
30. Alonso O, Loinaz C, Moreno E, Jiménez C, Abradelo M, Gómez R, et al. Advanced donor age increases the risk of severe recurrent hepatitis C after liver transplantation. ***Transpl Int*** 2005; 18: 902-907.
31. Feng S, Roberts J. An older liver in the hand, or a (possibly) younger liver in the bush? ***Am J Transplant*** 2005; 5: 425-427.
32. Gutiérrez E, Andrés A. Selection of donor and organ viability criteria: expanding donation criteria. ***J Ren Care*** 2007; 33: 83-88.

Ethical Approval

All manuscripts reporting the results of experimental investigations involving human subjects should include a statement confirming that informed consent was obtained from each subject or subject's guardian, after receiving approval of the experimental protocol by a local human ethics committee, or institutional review board. When reporting experiments on animals, authors should indicate whether the institutional and national guide for the care and use of laboratory animals was followed.