Septuagenarian and Octogenarian Donors Provide Excellent Liver Grafts for Transplantation

T. Darius, D. Monbaliu, I. Jochmans, N. Meurisse, B. Desschans, W. Coosemans, M. Komuta, T. Roskams, D. Cassiman, S. van der Merwe, W. Van Steenbergen, C. Verslype, W. Laleman, R. Aerts, F. Nevens, and J. Pirenne

ABSTRACT

Background. Wider utilization of liver grafts from donors ≥70 years old could substantially expand the organ pool, but their use remains limited by fear of poorer outcomes. We examined the results at our center of liver transplantation (OLT) using livers from donors ≥70 years old.

Methods. From February 2003 to August 2010, we performed 450 OLT including 58 (13%) using donors ≥70 whose outcomes were compared with those using donors <70 years old.

Results. Cerebrovascular causes of death predominated among donors ≥70 (85% vs 47% in donors <70; $P < .001$). In contrast, traumatic causes of death predominated among donors <70 (36% vs 14% in donors ≥70; $P = .002$). Unlike grafts from donors <70 years old, grafts from older individuals had no additional risk factors (steatosis, high sodium, or hemodynamic instability). Both groups were comparable for cold and warm ischemia times. No difference was noted in posttransplant peak transaminases, incidence of primary nonfunction, hepatic artery thrombosis, biliary strictures, or retransplantation rates between groups. The 1- and 5-year patient survivals were 88% and 82% in recipients of livers <70 versus 90% and 84% in those from ≥70 years old ($P = .705$). Recipients of older grafts, who were 6 years older than recipients of younger grafts ($P < .001$), tended to have a lower laboratory Model for End-Stage Liver Disease score ($P = .074$).

Conclusions. Short and mid-term survival following OLT using donors ≥70 yo can be excellent provided that there is adequate donor and recipient selection. Septuagenarians and octogenarians with cerebrovascular ischemic and bleeding accidents represent a large pool of potential donors whose wider use could substantially reduce mortality on the OLT waiting list.

THE GAP between the limited number of donor organs and the number of patients referred for liver transplantation (OLT) has continued to increase over the last decade, resulting in longer waiting times and higher mortality rates. Extended criteria donors (ECD), donation after circulatory death (DCD), and living donation have been increasingly used to overcome this problem.

Among ECD, elevated and uncorrected serum sodium, prolonged intensive care (ICU) stay, abnormal liver tests, hemodynamic instability, split grafts, cardiac arrest, advanced (>30%) macrovesicular steatosis, and advanced donor age have all been reported to negatively influence graft survival.[1] For this reason, the use of liver grafts from donors ≥70 years old has remained fairly limited considering the large pool of these potential donors.[2] We have been quite liberal in the acceptance of older liver grafts at our center. The objective of this retrospective single center study was therefore to analyze the outcomes of OLT using

From the Department of Abdominal Transplant Surgery (T.D., D.M., I.J., N.M., B.D., W.C., R.A., J.P.), Department of Pathology (M.K., T.R.), and Department of Hepatology (D.C., S.v.d.M., W.V.S, C.V., W.L., F.N.), University Hospitals Leuven, Leuven, Belgium.

Address reprint requests to Jacques Pirenne, MD, PhD, Department of Abdominal Transplant Surgery, University Hospitals Leuven, Herestraat 49, B-3000 Leuven, Belgium. E-mail: jacques.pirenne@uzleuven.be

0041-1345/–see front matter
http://dx.doi.org/10.1016/j.transproceed.2012.09.076

"older" septuagenarian and octogenarian donors, and to compare their outcome with those using "younger" donors.

MATERIALS AND METHODS

We reviewed all OLT performed at our center between February 2003 and August 2010. Outcomes of OLT from donors ≥70 were compared with those from donors <70. Donor liver acceptance was based upon standard clinical, biochemical, anatomical, and—if necessary—histologic criteria. We analyzed a series of relevant donor, surgical, and recipient characteristics and posttransplant endpoints prospectively entered in our unit database. Donor characteristics included age, gender, cause of death, cardiac arrest, hypotensive period, inotropic support, type of preservation solution, and procurement region (regional, national, international). At the time of procurement, liver biopsies were not obtained routinely, but only processed when the macroscopic aspect of the liver appeared to be abnormal. Recipient characteristics included primary liver disease, Model for End-Stage Liver Disease (MELD) score, age, and gender.

Surgical characteristics included cold ischemia time (from cold flush in the donor to start of vascular anastomosis in the recipient) and warm ischemia time (anastomosis time) and duration of surgery. Posttransplant endpoints included peak transaminase (a surrogate of ischemia reperfusion injury), incidence of primary nonfunction, hepatic artery thrombosis, biliary complications, acute rejection episodes, the need for retransplantation and eventually 1- and 5-year graft and patient survivals. Given the well-established impact of donor age on hepatitis C virus (HCV) recurrence, we separately analyzed the results of transplantation of older liver grafts into HCV recipients.[3,4]

Statistical analysis used SPSS 19.0 (SPSS, Chicago, Ill). Mean values were compared using Student's *t*-test or Mann-Whitney rank sum test where appropriate proportions were compared with *z*-tests with Yates corrections. Survival curves were produced using the Kaplan–Meier method. $P < .05$ were considered to be significant.

RESULTS

During the 7-year study period, we performed 450 OLT including 58 livers (13%) from donors ≥70 years old. Early in the series, livers from donors ≥70 procured by our team were frequently turned down by other centers based on the advanced age and eventually allocated as "center offers" or "rescue allocation." They were then accepted for selected patients, including older recipients, individuals thought to be at a disadvantage on the waiting list for various reasons, recipients for whom the MELD score was thought not to reflect accurately their mortality risk, patients with hepatocellular carcinoma, and so on. Later in the series, careful use of older liver grafts became more generally accepted nationally and within Eurotransplant; as a result, these livers were more frequently, patient-allocated (standard allocation).

Donor Characteristics

The median age of septuagenarian and octogenarian donors was 77 years (Table 1). The youngest was 70 years. Fifteen (26%) were ≥80 with the oldest being 89. Cerebrovascular ischemia or nontraumatic bleeding and cerebral trauma represented 85% and 14% of the causes of death among the ≥70 versus 47% and 36% in donors <70 years old. Seventy-one percent of the liver grafts originating from donors ≥70 years old were retrieved by our procurement team in our donor region versus 31% for the donors <70 years old ($P < .001$). That the majority of these older grafts were procured in our donor region reflects our center policy of considering all brain-dead patients as potential liver donors independent of age. Liver tests in donors ≥70 years old were normal: Median aspartate aminotransaminase (AST) values was 29 IU/L (range, 10–95) and median total bilirubin 0.63 mg/dL (range, 0.22–1.60). University of Wisconsin (UW) preservation solution was used in 90% versus 66% in donors ≥70 versus <70 years old, respectively ($P < .001$); histidine-tryptophan-ketoglutarate (HTK) in 10% versus 34%, respectively ($P = .007$).

Recipient Characteristics

The median age of recipients of a liver ≥70 years old was 6 years older than that of recipients of a younger liver (61 vs

Table 1. Donor Characteristics

	Donors ≥70 Years ($n = 58$)	Donors <70 Years ($n = 392$)	*P*
Donor age, median (range), yrs	77 (70–89)	48 (2–69)	<.001
Gender, male/female (%)	25/33 (43%/57%)	223/169 (57%/43%)	.068
Donation after brain death/donation after circulatory death	58/0 (100%/0%)	366/26 (93%/7%)	.085
Cerebrovascular death, *n* (%) (ischemic/nontraumatic bleeding)	49 (85%)	185 (47%)	<.001
Trauma death, *n* (%)	8 (14%)	140 (36%)	.002
Cardiac arrest, *n* (%)	3 (5%)	61 (16%)	.056
Hypotensive period, *n* (%)	19 (33%)	92 (24%)	.171
Mild inotrope support, *n* (%)	39 (67%)	173 (44%)	.002
Sodium, median (range), mmol/L (normal range, 145–145)	144 (132–161)	147 (124–174)	.033
Aspartate aminotransferase median (range), IU/L (normal, <32)	29 (10–95)	44 (10–278)	.012
Total bilirubin, median (range), mg/dL (normal, <1.00)	0.63 (0.22–1.60)	0.58 (0.6–2.97)	.067
University of Wisconsin preservation solution	52 (90%)	257 (66%)	<.001
Hystidine tryptophan ketoglutarate solution	6 (10%)	110 (28%)	.007
Regional offer (procurement by our center)	41 (71%)	123 (31%)	<.001
National offer (procurement by other Belgian center)	12 (21%)	150 (38%)	.014
International offer (procurement outside Belgium)	5 (8%)	119 (31%)	.001

Table 2. Recipient Characteristics

	Donors ≥ 70 Years (n = 58)	Donors < 70 Years (n = 392)	P
Age, median (range), yrs	61 (45–75)	55 (6 months–77 years)	<.001
Gender, male/female, n (%)	33/25	243/149	.550
Lab MELD score, median (range)	14 (6–42)	16 (4–52)	.074
Matched MELD score, median (range)	22 (20–25)	25 (20–30)	.616
Indications for Liver transplantation, n (%)			
Hepatocellular carcinoma	23 (40%)	95 (24%)	<.001
Post-ethyl alcohol liver disease	17 (29%)	81 (21%)	.187
Hepatocellular carcinoma + postethyl alcohol liver disease	10 (17%)	25 (6%)	.009
Cryptogenic liver disease	4 (7%)	14 (4%)	.398
Hepatitis C cirrhosis and hepatocellular carcinoma	5 (9%)	31 (8%)	.944
Hepatitis C cirrhosis without hepatocellular carcinoma	0 (0%)	13 (3%)	.324
Others	7 (15%)	137 (41%)	<.001
Primary transplants/retransplants, n (%)	55/3 (95%/5%)	358/34 (91%/9%)	.516

55 years old; $P < .001$; Table 2). The median laboratory MELD score tended to be lower in recipients of older versus younger grafts (14 vs 16; $P = .074$). The average matched MELD score did not differ between groups (22 vs 25; $P = .616$). Older liver grafts were more frequently allocated to recipients with hepatocellular carcinoma (40% vs 24%; $P < .001$).

Surgical Characteristics

Median cold and warm ischemia times did not differ between recipients of younger versus older liver grafts: 8 hours 32 minutes versus 8 hours 3 minutes ($P = .788$) and 46 versus 47 minutes ($P = .841$) respectively (Table 3). Duration of surgery, graft size (whole graft versus split graft), use of venovenous bypass, and type of biliary anastomosis were comparable between the 2 groups.

Posttransplant Outcome

Median peak AST and ALT in recipients of a liver ≥70 and <70 were not different: 597 IU/L (range, 59–12,802) and 688 IU/L (range, 47–5071) versus 648 IU/L (range, 81–9980) and 601 IU/L (range, 46–8898; $P = .590$ and $P = .890$, respectively; Table 4). No hepatic artery thrombosis was observed in recipients of older grafts. Although no primary nonfunction was seen in recipients of older grafts, 2 suffered prolonged graft dysfunction: One was successfully treated with 3 sessions of molecular absorbent recirculating system (MARS) and another recovered spontaneously.[5,6] The incidence of biliary strictures was comparable in both groups.

The median follow-up was 35 months (range, 3–90). The 1- and 5-year liver graft survivals were comparable between the 2 groups: 88% and 79% for recipients of grafts ≥70 versus 89% and 83% for recipient of grafts <70 years old ($P = .637$; Fig 1). The 1- and 5-year patient survivals were also comparable between the 2 groups: 88% and 82% for recipients of grafts ≥70 versus 90% and 84% for recipients of grafts <70 years old ($P = .705$; Fig 2).

HCV-Positive Patients

Among the 5 (8%) recipients of older livers, who were transplanted due to HCV cirrhosis, 4 (80%) developed biopsy-proven HCV recurrence at 1, 9, 12 and 24 months post-OLT. They required treatment with peginterferon alfa-2a and ribavirin. In contrast, 44 (11%) of recipients of liver grafts from donors <70, who were transplanted for HCV, only 16 (36%) developed biopsy-proven HCV recurrence needing antiviral therapy with peginterferon alfa-2a and ribavirin.

DISCUSSION

Over the last 20 years, advances in donor management, preservation, recipient selection, surgical techniques, perioperative care, and immunosuppression have significantly improved the results of OLT. Over the same period the waiting list has increased dramatically. To decrease the gap

Table 3. Surgical Characteristics

	Donors ≥70 Years (n = 58)	Donors <70 Years (n = 392)	P
Surgical time, median (range), hrs	4h57 (3h00–9h03)	5h05 (2h38–11h05)	.380
Graft size, full/split graft, n (%)	58/0 (100%/0%)	377/15 (96%/4%)	.261
Venovenous bypass, n (%)	58 (100%)	381 (97%)	.402
Biliary anastomosis, n (%)			
Duct-to-duct	55 (95%)	349 (89%)	.260
Hepaticojejunostomy	3 (5%)	43 (11%)	.260
Cold ischemia time, median (range), hrs	8h03 (3h34–13h44)	8h32 (3h31–13h45)	.788
Warm ischemia time, median (range), min	47 (31–88)	46 (22–103)	.841

Table 4. Posttransplant Endpoints

	Donors ≥ 70 Years (n = 58)	Donors < 70 Years (n = 392)	P
Follow up, median (range), mos	35 (3–90)	35 (3–90)	
Peak aspartate transaminase, median (range), IU/L (normal, <32)	597 (59–12,802)	648 (81–9980)	.590
Peak alanine transaminase, median (range), IU/L (normal, <31)	688 (47–5071)	601 (46–8898)	.890
Primary nonfunction, n (%)	0 (0%)	2 (0.5%)	.608
Hepatic artery thrombosis, n (%)	0 (0%)	9 (2%)	.509
Biliary strictures, n (%)	7 (12%)	75 (19%)	.263
Acute cellular rejection, n (%)	10 (17%)	66 (17%)	.912
Retransplantation, n (%)	1 (2%)	18 (5%)	.506

between supply of and demand for liver grafts, multiple strategies have emerged: More liberal use of ECD and DCD donors and living donation. Unlike for kidneys, there is no universally accepted definition of an ECD liver. Conceptually liver grafts originating from ECD donors are deemed to be at higher risk of primary nonfunction and/or graft dysfunction.[7–9] Donor factors that have a negative influence on graft function and survival include: advanced donor age, hepatic steatosis (>30%), prolonged cold ischemia time, abnormal liver tests, nontraumatic cause of death, uncorrected hypernatremia, vasopressor requirement, prolonged ICU stay, extended duration of liver hypoperfusion because of cardiac dysrhythmia or cardiac arrest, and split grafts.[9–14] Despite being at greater risk, the use of these grafts is justified in view of the increased waiting list mortality and their better outcomes compared with no transplantation.

Important factors in the outcome of liver grafts in general, and particularly in the outcome of higher risk grafts, is adequate donor management with particular attention to blood glucose monitoring and insulin substitution. Rapid, efficient procurement with minimal manipulation of the donor liver with rapid cooling are also of paramount importance.[15,16] Finally, recipient factors (the "environment" where the graft is transplanted) may also play a role in the outcome of liver grafts in general, and of higher risk grafts in particular.[16]

Brain death owing to cerebrovascular ischemia or nontraumatic bleeding was more frequent among donors >70 years old; however, these potential donors are frequently underreported based on the erroneous assumption by anesthetists or intensivists that advanced donor age per se is an absolute contraindication for donation. In addition, transplant teams may be reluctant to use older livers due to fear of poorer outcomes; advanced age is a well-known risk factor for inferior outcomes. A series of single center studies have shown donor age to be associated with poorer initial function and lower graft and recipient survivals.[11,13,17] Due to senescence mechanisms, older organs in general show less functional reserve, greater susceptibility to damage and reduced repair capacities.[8] In particular, older livers are more susceptible to endothelial cell injury caused by cold ischemia due to decreased adenosine triphosphate synthesis after reperfusion, which can decrease synthetic functions and negatively affect regenerative

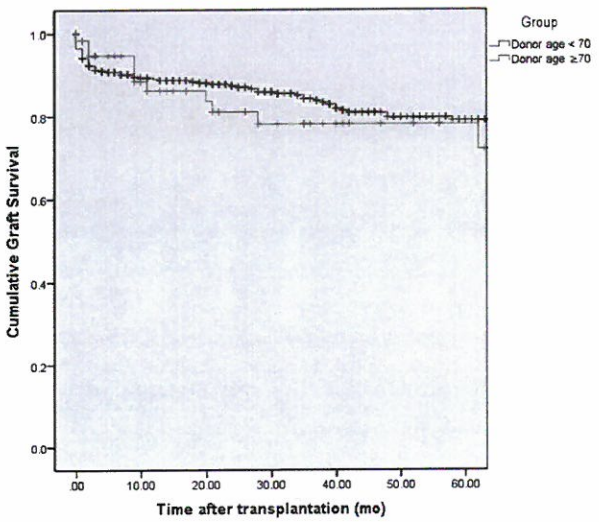

Fig 1. Graft survival after liver transplantation according to donor age.

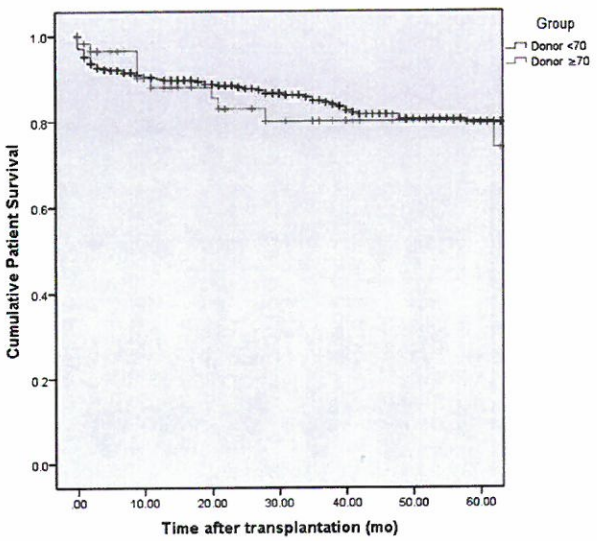

Fig 2. Patient survival after liver transplantation according to donor age.

capacity.[12] However according to recent literature, age-related morphological, ultrastructural and functional alterations in the liver are minimal, in contrast with the heart, lung and kidneys.[18] Overall liver function remains well preserved owing to the effective counterbalance by its large functional reserve, regenerative capacity and dual blood supply.[18] The risk of prolonged cold ischemia time, an independent risk factor for liver preservation injury, increases with donor age.[12] Therefore the combination of advanced donor age and prolonged cold ischemia may be particularly deleterious and should be avoided. Warm ischemia should also be minimized since it has been shown that it intensifies cold ischemic injuries and vice versa.[12]

Not only single-center data, but also international registries have concurred to demonstrate that donor age is a risk factor for graft failure and recipient mortality. In an analysis of the European Liver Transplant Registry, donor age >60 years significantly increased the 3-month patient mortality.[19] In an analysis of the Scientific Registry of Transplant Recipients, donor age >40, and particularly >60, was strongly associated with graft failure.[20]

In stark contrast to these international data, the current single-center study demonstrated that graft and patient survival rates up to 5 years posttransplantation using donors ≥70 years old can be comparable to results obtained using younger donors. No difference in the incidence of posttransplant complications, PNF, graft dysfunction or hepatic artery thrombosis was noted in our series, consistent with other recently reported single-center series (Table 5).[1,10,21–25]

How can the results of OLT using older donors be optimized? An essential strategy when using older grafts is to exclude the presence of additional risk factors for poorer graft and recipient outcomes.[1,7,8,14] We were by far more strict in our acceptance criteria for older than younger donors. Unlike younger donors, liver tests and serum sodium were almost always normal among those ≥70 years old. To avoid additional ischemic trauma, we did not accept an older donor who had suffered a cardiac arrest. For the same reasons we turned down potential DCD donors above the age of 60 yr. To avoid a rewarming injury during the back table work, none of the older donor organs were split or reduced. Because steatosis is associated with increased rates of primary non-function and initial poor function, we routinely avoided the use of old, overtly steatotic grafts.[12] Steatosis was evaluated by ultrasound before donation (when available), by macroscopic examination at the time of procurement and—in case of uncertainty—by biopsy. Not only donor selection, but also optimal management to maintain a normal circulation and oxygenation were essential for these outcomes of older grafts: Aggressive correction of hypernatremia, adequate fluid balance, donor blood glucose management, insulin substitution, and hemodynamic stability were all essential. Equally as important as donor selection and management is efficient, straightforward procurement by experienced surgeons with as little manipulation of the donor organs as possible, rapid aortic cannulation and cold perfusion, abundant topical cooling and prompt hepatectomy. Stewart et al[26] recently showed that HTK preservation was associated with a 1.2-fold greater odds of early (<30 days) graft loss compared with UW preservation with more pronounced effects observed among grafts exposed to >8 hours of cold ischemia or obtained from DCD donors, or from individuals ≥70. Consistent with these observations, we routinely use UW solution for procurements, including those from older donors. The majority of these older grafts were procured by our own team and therefore perfused with UW, which was not necessarily the case for imported liver grafts. Because longer ischemia times are associated with greater rate of biliary complications and because older livers are more prone to ischemic damage, their cold ischemia time should be kept to a minimum. We have cold ischemia times short (around 8 hours) for all OLT independent of donor age. Given the adverse interactions between cold and warm ischemia times, the warm ischemia (anastomosis) time should be kept short too. No difference in the incidence of biliary strictures was observed between recipients of older versus younger livers.

Another important factor to optimize the outcomes of these older grafts is adequate recipient selection. Whenever

Table 5. Single-Center Experiences of Liver Transplantation Using Grafts From Donors > 70 Years Old

Author, Year	Number of Patients	Donor Age (yrs) (range)	Patient Survival	Graft Survival
Sukru, 1996	36	≥70 (70–84)	1y: 91%	1y: 85%
Grazi, 2001	36	≥70 (70–87)	1y: 77.4%	1y: 73.3%
Cescon, 2003	17	≥80 (80–87)	2y: 100%	
			3y: 75%	
Nardo, 2004	30	≥80	6m: 93.3%	6m: 90%
Kim, 2004	25	≥70 (70–80)	1y: 95.4%	1y: 82.7%
			3y: 89.8%	3y: 71.7%
Gastaca, 2005	55	>70	1y: 93.8%	1y: 92.6
			3y: 90.6%	3y: 89.4
Petridis, 2008	10	≥80 (80–93)	1y: 80%	1y: 80%
			3y: 40%	
Darius, 2011	58	≥70 (70–89)	1y: 88%	1y: 86%
			5y: 80%	5y: 78%

possible, we allocated older grafts to more stable patients who we thought would better tolerate some degree of liver graft dysfunction. These patients displayed lower laboratory MELD scores; among them were HCC patients who are disadvantaged by the allocation system. However, a substantial percentage of older livers were successfully used in severely sick recipients with higher laboratory MELD scores or even for retransplantations. The use of older liver grafts in recipients transplanted because of HCV-related cirrhosis is a well-known risk factor for inferior outcomes.[3,4,15] In our study, we were obliged to allocate older liver grafts to five HCV recipients who were in too critical a situation to wait for a "younger" graft. Eighty percent of them developed HCV recurrences requiring antiviral treatment within 2 years posttransplant, confirming that HCV patients should—ideally—not receive liver grafts from older donors.

Older livers are usually proportionately smaller than livers from younger donors, particularly those from female donors (data not shown), reported previously.[27] This factor should be taken into account when selecting recipients to avoid a small-for-size syndrome. The macroscopic aspect of these livers are quite characteristic: A typically darker, more brownish aspect compared with younger livers due to accumulation of lipofuscine pigments in hepatocytes.[27] They also often display more or less diffuse white spot areas or plaques; which represent only superficial changes owing to fibrosis in the capsule of Glisson. Younger procurement surgeons should be familiar with these typical age-related macroscopic changes since they represent by no means, a contraindication to liver donation.

That livers from septuagenarian and even octogenarian donors can function well posttransplantation confirms the relative intrinsic resistance of livers to the normal process of aging. There are even anecdotal cases of successful transplantation of livers from nonagenarian donors.[28] This resistance to aging is probably due in part to the unique regenerative potential of the liver. A biopsy at 2 weeks post-OLT in the recipient of the oldest liver graft in our series (89 years old) showed proliferation of small-sized hepatocytes with a compact growth pattern, suggesting liver parenchymal regeneration (Fig 3). In addition, the proliferative marker Ki-67 showed nuclear positivity in the area of parenchymal regeneration. These features suggested that even the oldest liver grafts (89 years old) are capable of hepatocyte proliferation. In addition and in contrast to all other visceral arteries, the celiac trunk rarely displays signs of advanced atherosclerosis. In many of these older donors, kidneys were not transplantable due to advanced calcifications of the renal arteries whereas the hepatic artery had remained remarkably supple.

Kidney grafts from older donors are more vulnerable to rejection than those from younger individuals.[29] Indeed, in the Eurotransplant Senior Program, allocation of kidneys from donors aged ≥65 to recipients ≥65 years old led to a 5%–10% higher rejection rate than observed among recipients of younger organs.[25–30] Similarly, de Fijter et al[31] demonstrated an increased cumulative incidence of acute rejection episodes in patients receiving a kidney from donors >50. In contrast to these kidney studies, our current analysis demonstrated that older liver grafts were not more susceptible to rejection; the incidence of acute rejection episodes (17%) was identical in both groups. Although the incidence of rejection was not greater, we cannot exclude that recovery from rejection may last longer among recipients of older livers, owing to their inferior functional reserve. In 1 case in our series, a patient who developed a severe rejection response showed complete histologic reso-

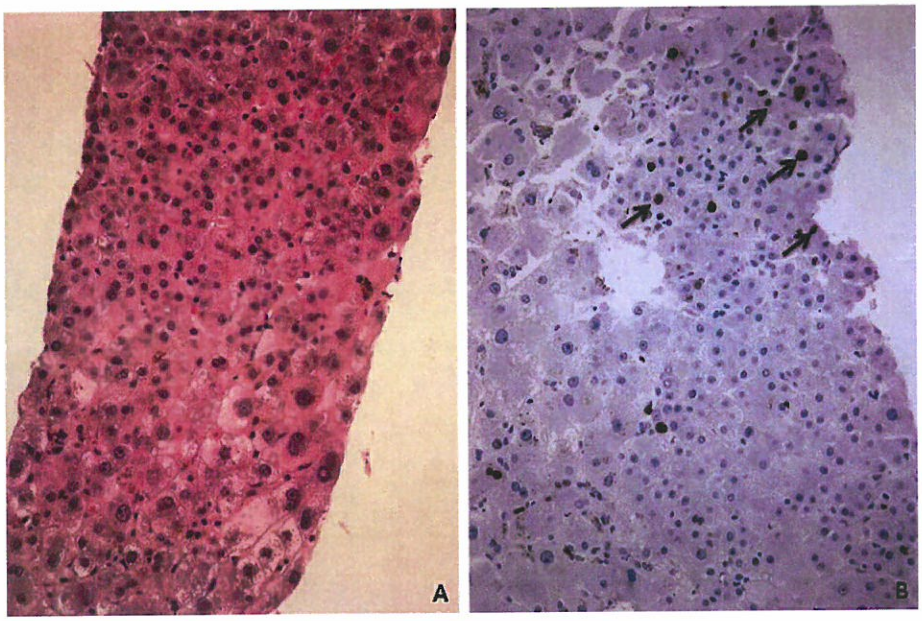

Fig 3. Liver needle-biopsy taken 2 weeks after liver transplantation with an 89-year-old liver graft. **(A)** Liver parenchyma composed of ballooned, pale-colored hepatocytes with an atypical nuclei indicating preservation damage (lower side), and small-sized hepatocytes proliferating with a compact growth pattern indicating liver regeneration (upper side) (×200; hematoxylin-eosin). **(B)** Ki-67–positive nuclei (arrow) are only seen in the area of liver parenchymal regeneration (×200; Ki-67).

lution of the episodes after treatment, although the liver function remained profoundly disturbed, requiring retransplantation.

Although brain death owing to cerebrovascular ischemia or nontraumatic bleeding is frequent among patients >70 years old, this potential group of donors remains largely underused, representing a small percentage of the effective donor pool. Wider use of these grafts could dramatically reduce mortality on the waiting list. Advanced donor age per se should no longer be seen to be an absolute contraindication to liver donation and transplantation. Anesthetists and intensivists in charge of potential donors should be encouraged not to exclude donors based solely on chronologic age. On the contrary, these donors should be systematically reported to a transplant center and managed with great care. Often in situ macroscopic inspection of the liver by a surgeon experienced in procurement and transplantation can be decisive for the final acceptance or discard of a particular organ.

In conclusion, the short-term (1-year) and mid-term (5 year) results of OLT using septuagenarian and octogenarian livers can be similar to those of recipients of younger grafts, provided that (1) donors are strictly selected (in particular absence of additional risk factors) and optimally managed; (2) the procurement is performed rapidly with little manipulation and rapid cooling; (3) cold and warm ischemia times are kept short; and (4) recipients are adequately selected. Given the absence of 10-year results, it seems wiser to allocate older livers to elderly recipients who have naturally shorter lifespans.

REFERENCES

1. Petridis I, Gruttadauria S, Nadalin S, et al: Liver transplantation using donors older than 80 years: a single-center experience. Transplant Proc 40:1976, 2008
2. Pirenne J, Monbaliu D, Van Gelder F, et al: Liver transplantation using livers from septuagenarian and octogenarian donors: an underused strategy to reduce mortality on the waiting list. Transplant Proc 37:1180, 2005
3. Mutimer DJ, Gunson B, Chen J, et al: Impact of donor age and year of transplantation on graft and patient survival following liver transplantation for hepatitis C virus. Transplantation 81:7, 2006
4. Russo MW, Galanko JA, Zacks SL, et al: Impact of donor age and year of transplant on graft survival in liver transplant recipients with chronic hepatitis C. Am J Transplant 4:1133, 2004
5. Laleman W, Wilmer A, Evenepoel P, et al: Effect of the molecular adsorbent recirculating system and Prometheus devices on systemic haemodynamics and vasoactive agents in patients with acute-on-chronic alcoholic liver failure. Crit Care 10:R108, 2006
6. Darius T, Monbaliu D, Aerts R, et al: Rescue of a marginal liver graft by sequential treatment with molecular adsorbent recirculating system and transjugular intrahepatic portosystemic shunt: a case report. Transplant Proc 41:3427, 2009
7. Cameron AM, Ghobrial RM, Yersiz H, et al: Optimal utilization of donor grafts with extended criteria: a single-center experience in over 1000 liver transplants. Ann Surg 243:748, 2006
8. Gordon BS, Busuttil RW: Optimal utilization of extended hepatic grafts. Surg Today 39:746, 2009
9. Durand F, Renz JF, Alkofer B, et al: Report of the Paris consensus meeting on expanded criteria donors in liver transplantation. Liver Transpl 14:1694, 2008
10. Gastaca M, Valdivieso A, Pijoan J, et al: Donors older than 70 years in liver transplantation. Transplant Proc 37:3851, 2005
11. Ploeg RJ, D'Alessandro AM, Knechtle SJ, et al: Risk factors for primary dysfunction after liver transplantation-a multivariate analysis. Transplantation 55:807, 1993
12. Busuttil RW, Tanaka K: The utility of marginal donors in liver transplantation. Liver Transpl 9:651, 2003
13. Busquets J, Xiol X, Figueras J, 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 71:1765, 2001
14. Schemmer P, Nickkholgh A, Hinz U, et al: Extended donor criteria have no negative impact on early outcome after liver transplantation: a single-center multivariate analysis. Transplant Proc 39:529, 2007
15. Kim DY, Moon J, Island ER, et al: Liver transplantation using elderly donors: a risk factor analysis. Clin Transplant 25:270, 2011
16. Schemmer P, Schoonhoven R, Swenberg JA, et al: Gentle organ manipulation during harvest as a key determinant of survival of fatty livers after transplantation in the rat. Transpl Int 12:351, 1999
17. Rull R, Vidal O, Momblan D, et al: Evaluation of potential liver donors: limits imposed by donor variables in liver transplantation. Liver Transpl 9:389, 2003
18. Singhal A, Sezginsoy B, Ghuloom AE, et al: Orthotopic liver transplant using allografts from geriatric population in the United States: is there any age limit? Exp Clin Transplant 8:196, 2010
19. Burroughs AK, Sabin CA, Rolles K, et al: 3-month and 12-month mortality after first liver transplant in adults in Europe: predictive models for outcome. Lancet 367:225, 2006
20. Feng S, Goodrich NP, Bragg-Gresham JL, et al: Characteristics associated with liver graft failure: the concept of a donor risk index. Am J Transplant 6:783, 2006
21. Kim DY, Cauduro SP, Bohorquez HE, et al: Routine use of livers from deceased donors older than 70: is it justified? Transpl Int 18:73, 2005
22. Grazi GL, Cescon M, Ravaioli M, et al: A revised consideration on the use of very aged donors for liver transplantation. Am J Transplant 1:61, 2001
23. Cescon M, Grazi GL, Ercolani G, et al: Long-term survival of recipients of liver grafts from donors older than 80 years: is it achievable? Liver Transpl 9:1174, 2003
24. Emre S, Schwartz ME, Altaca G, et al: Safe use of hepatic allografts from donors older than 70 years. Transplantation 62:62, 1996
25. Nardo B, Masetti M, Urbani L, et al: Liver transplantation from donors aged 80 years and over: pushing the limit. Am J Transplant 4:1139, 2004
26. Stewart ZA, Cameron AM, Singer AL, et al: Histidine-Tryptophan-Ketoglutarate (HTK) is associated with reduced graft survival in deceased donor livers, especially those donated after cardiac death. Am J Transplant 9:286, 2009
27. Schmucker DL: Age-related changes in liver structure and function: implications for disease? Exp Gerontol 40:650, 2005
28. Filipponi F, Romagnoli J, Urbani L, et al: Transplantation of a ninety-three-year-old donor liver. Case report. Hepatogastroenterology 50:510, 2003
29. Tullius SG, Milford E: Kidney allocation and the aging immune response. N Engl J Med 364:1369, 2011
30. Frei U, Noeldeke J, Machold-Fabrizii V, et al: Prospective age-matching in elderly kidney transplant recipients–a 5-year analysis of the Eurotransplant Senior Program. Am J Transplant 8:50, 2008
31. de Fijter JW, Mallat MJ, Doxiadis II, et al: Increased immunogenicity and cause of graft loss of old donor kidneys. J Am Soc Nephrol 12:1538, 2001