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Liver Transplantation from Donors Aged 80 Years and Over: Pushing the Limit

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Older donors are a growing part of the total donor pool but no definite consensus exists on the limit of age for their acceptance. From November 1998 to January 2003, in a retrospective case–control multicenter study, we compared the outcome of 30 orthotopic liver transplantations (OLTs) with octogenarian donors and of 60 chronologically correlated OLTs performed with donors <40 years. The percentage of refusal was greater among older than younger donors (48.2 vs. 14.3%; $p < 0.001$). Cold ischemia was significantly shorter in the older than younger groups. Recipients with hepatocarcinoma and older age received octogenarian grafts more frequently. No differences were seen in post-operative complications and 6-month graft and patient survival. However, long-term survival was lower in patients transplanted with octogenarian donors ($p = 0.04$). Interestingly, the mortality related to hepatitis C recurrence was greater in patients with octogenarian donors. Accordingly, the long-term survival of HCV-positive patients who received older grafts was lower than those receiving younger grafts ($p = 0.05$). Octogenarian livers can be used safely but a careful donor evaluation and a short cold ischemia are required to prevent additional risk factors. However, hepatitis C recurrence is associated with a greater mortality in patients who received octogenarian grafts raising concerns whether to allocate these livers to HCV-positive recipients.

Key words: Hepatitis C, liver transplantation, old donors

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Introduction

The increasing number of patients listed for liver transplantation and the persistent shortage of potential donors have led to a mortality rate in the waiting list close to 20% per year (1,2). An immediate and realistic policy to expand the donor pool is to transplant livers from older donors who were previously discarded (3,4). However, no definite consensus exists on the limit of age to establish a priori whether a liver donor can be transplanted or refused. Until a decade ago, the accepted limit of donor age was generally 60 years and older donors were almost exclusively evaluated for urgent procedures (5–11). The general lack of enthusiasm to transplant livers from older donors was based on the evidence that their use was associated with a higher risk of initial poor function (IPF) or primary graft nonfunction (PNF) (12–16) and with a greater risk of transmission of occult tumors (17,18).

In the last decade, however, a greater willingness to use older organs has been shown by transplant teams. Indeed, donors >65 years have become a substantial source of organs, increasing from 0.1% of the donor pool in 1988 to 8.5% in 2002 (United Network for Organ Sharing report). Interestingly, the 1-year graft and patient survival of liver transplantation from donors >65 years old was only slightly worse than those observed for patients who received livers from younger donors (50–64 years) (72.0% and 80.7% vs. 77.2% and 83.3%, respectively) (UNOS report). In the European Liver Transplant Registry, the 1-year survival of the patients transplanted from 1988 to 2001 with grafts retrieved from donors >65 years old was similar to the survival of the patients who received grafts from donors aged 55–65 years or grafts from donors aged <55 years (69%, 71%, and 75%, respectively). However, these data do not indicate the upper age limit of the donor livers which were transplanted. In more recent years, some reports have disclosed the possibility of pushing the upper donor age limit beyond 70 years old (3,19–21). Indeed, it has been shown that transplantation of livers from septuagenarian donors does not produce a decrease in the 1-year actuarial graft and patient survival (3,19). However, an

increase in long-term mortality and graft loss among orthotopic liver transplantations (OLTs) from donors aged over 70 has been reported by a Spanish group, suggesting that these donors should not be accepted routinely but used only in selected cases (20). Even grafts from donors older than 80 years have been transplanted with satisfactory results exclusively in elective settings. However, these data come from case reports (22–26) or from small series (4).

Based on these previous sporadic observations and because no clear guidelines exist regarding the criteria adopted in accepting grafts from older donors, the aim of the present study was to retrospectively compare, in a case–controlled multicenter study, the early- and long-term outcome of liver recipients transplanted with grafts procured from donors over 80 years old compared with those transplanted with grafts from donors less than 40 years old.

Materials and Methods

Study population

We designed a multicenter case–controlled study with a ratio 1:2. Between November 1998 and January 2003, 30 consecutive livers from donors >80 years old were transplanted at three different Italian Liver Transplant Centers (Bologna, Modena and Pisa). The mean age of the older donor group was 82.7 years (range 80–93). The control group consisted of 60 OLTs. In each center, the control cases were chronologically correlated, choosing the first transplants with livers from donors <40 years old performed before and after those using octogenarian grafts. The controls were also sex matched whenever possible. As the prevalence of females was, as expected, greater among the older than the younger donors, the number of transplants from female donors <40 years old was insufficient to match all the transplants from older donors. Thus, we were forced to use chronologically correlated transplants from male donors instead of transplants from female donors in 12 cases. The mean age of the younger donor group was 27.6 years (range 13–40). Re-transplantations, split-technique, multiorgan transplantation, and pediatric transplantations were excluded from the study.

Donor and pre-transplant recipient data

The general indications for acceptance of older donors were: (i) normal gross appearance and no relevant abnormalities at histology (for example: steatosis >30%, bridging fibrosis, presence of hepatitis); (ii) no alteration of liver function tests; and (iii) hemodynamic stability with use of low doses of vasopressors.

The following donor characteristics were evaluated: age, gender, cause of death, length of intensive care unit stay, systolic arterial pressure at the time of the procurement, number of hypotensive episodes defined as systolic arterial pressure <80 mmHg for more than 1 h, cardiac arrest, and vasopressive drug infusion prior to and during organ harvesting. The pre-harvesting donor values of aspartate-aminotransferase (AST), alanine-aminotransferase (ALT), total bilirubin, γ-glutamyl transferases (γ-GT), prothrombin activity (PT), activated partial thromboplastin time and sodium (Na^+) levels were also collected.

Liver biopsies from donors over 80 years old were carried out in all cases except three, while in the younger donor group liver biopsies were performed in 13 cases on the basis of the personal evaluation of the harvesting surgeon.

The following recipient data were collected: age, gender, indication for OLT and UNOS status according to the United Network of Organ Sharing classification.

Intra-operative and peri-operative data

The type of surgical procedure, warm and cold ischemic times, total surgical time, packed red blood cell and fresh frozen plasma infusion, and type of immunosuppression were considered for all patients.

Post-operative data

Liver function tests, bile output in the first post-operative week, PNF and IPF according to the definition by Strasberg et al. (14), intensive care unit (ICU) and total hospital stay, technical complications, and rejection episodes were collected for all the patients. The long-term patient and graft survival and the causes of death were also analyzed.

Statistical analysis

Results are expressed as mean $\pm$ standard deviation. Differences between means were evaluated using Student's *t*-test or the Mann–Whitney *U*-test when appropriate. Differences between the two groups were evaluated with the chi-square test with Yates' correction for continuity. Post-operative survival was computed from the day of OLT to the last follow-up visit or date of death. Survival rates were estimated by means of the life table method and differences between survivals compared using the long rank test. Data were managed with the use of SPSS software packaging 10.0 (SPSS Inc., Chigaco, IL, USA); p-values $\leq$0.05 were considered as statistically significant.

Results

Donor selection

In the study period, a total of 58 livers from donors >80 years old and 230 livers from donors aged <40 years old were referred to our three centers. The percentage of donor livers discarded was significantly greater in the older donor group than in the younger donor group [48.2% (28 livers) vs. 14.3% (33 livers); $p < 0.001$]. According to the study design, among the 197 younger donor livers transplanted (85.7%), 60 OLTs chronologically correlated and, whenever possible, sex matched were included in the present study.

Moderate to massive steatosis (11 vs. 4 cases, $p = 0.007$), HCV-related cirrhosis (5 vs. 1 cases, $p = 0.05$) and malignancies (4 vs. 0 cases, $p = 0.091$) undetected prior to graft harvesting were causes of organ refusal more frequently in the older than in the younger group. In contrast, livers were discarded for traumatic lesions more commonly among younger donors (5 vs. 0 cases, $p = 0.05$).

Donor demographic and clinical characteristics (Table 1)

No significant differences in the length of ICU stay, the number of patients with hypotensive episodes or cardiac arrests and amounts of dopamine infusion were found between the two groups. In contrast, the older group showed a greater incidence of cerebrovascular accidents ($p < 0.001$) and a lower incidence of trauma than the younger group ($p < 0.001$).

Table 1: Donor demographic, clinical characteristics and biochemical data

	Older group ≥80 years (n = 30)	Younger group ≤40 years (n = 60)	p
Age (years)	82.3 ± 3.1	27.6 ± 7.94	<0.001
Gender (M/F)	10/20	32/28	NS
Cause of death			
Cerebrovascular	24 (80%)	21 (35%)	<0.001
Trauma	6 (20%)	39 (65%)	<0.001
ICU stay (days)	3 ± 2.6	3 ± 3.5	NS
Donors with hypotensive episodes	7 (23.3%)	18 (30%)	NS
Donor with cardiac arrest	1 (3.3%)	9 (15%)	NS
Dopamine infusion (γ/kg/min)	4 ± 3.9	5.8 ± 4.4	NS
ALT (U/L)	25.8 ± 21.6	65.7 ± 70.4	<0.001
AST (U/L)	38 ± 26.1	82 ± 76.9	<0.001
Total bilirubin (mg/dL)	0.7 ± 0.3	1.4 ± 2.6	0.03
PT (%)	80.2 ± 18.9	75.8 ± 17	NS
aPTT (s)	37.7 ± 9.9	36.9 ± 15.9	NS
γ-GT (U/L)	61.8 ± 80.7	77 ± 184	NS
Serum Na^+	146.9 ± 7.9	146.8 ± 7.5	NS

Table 2: Intra-operative and peri-operative data

	Older group ≥80 years (30 pts)	Younger group ≤40 years (60 pts)	p
Preservation solution			
UW	15 (50%)	26 (43.3%)	NS
Celsior	15 (50%)	34 (56.7%)	
Technique			
Piggy-Back	19 (63.3%)	38 (63.3%)	NS
Conventional	11 (36.7%)	22 (36.7%)	
Cold ischemia time (min)	449 ± 129	563 ± 231	0.022
Warm ischemia time (min)	57.4 ± 15.9	49.1 ± 18.8	NS
Total operation time (min)	438 ± 90	443 ± 94	NS
PRBC transfusion (cc)	2273 ± 1982	1984 ± 2082	NS
FFP transfusion (cc)	2168 ± 1489	2334 ± 1325	NS
Immunosuppression			
Cyclosporine	21 (70%)	37 (61.7%)	NS
Tacrolimus	9 (30%)	23 (38.3%)	

UW: University of Wisconsin; PRBC: packed red blood cell; FFP: fresh frozen plasma.

Among the biochemical data, the younger donors presented significantly greater serum transaminase and total bilirubin levels before liver procurement than those measured in the older donors. This finding likely reflects a stricter selection among the older donors, who were discarded also on the basis of altered liver function tests, and the higher prevalence in younger donors who died as a result of trauma. No significant differences in PT, aPTT, γ-GT and serum Na^+ levels were found between the two groups.

In the older donor group a liver biopsy was performed in all but three grafts with a macroscopic appearance judged to be optimal by the harvesting surgeon. Liver histology appeared normal in 14 cases and showed a mild macrovescicular steatosis (less than 30%) in 13 cases. In the younger donor group, liver biopsies were performed in 13 cases showing a mild macrovescicular steatosis in four grafts and a normal liver histology in the remaining donors.

Intra-operative and peri-operative data (Table 2)

No differences between the two groups were seen in the type of preservation solution, surgical procedure, warm ischemic time and total operation time, intra-operative transfusion of homologous packed red blood cell and fresh frozen plasma or type of immunosuppression. In contrast, the cold ischemic time was significantly shorter in the older (449 ± 129 min) than in the younger donor group (563 ± 231 min) (p = 0.022).

Recipient demographic and clinical characteristics (Table 3)

The age of the patients receiving grafts from octogenarian donors (52.5 ± 9.4 years) was significantly higher than that of recipients transplanted with livers from younger donors (46.7 ± 10.5 years) (p = 0.012).

No differences between the two groups were seen for gender and UNOS status. Three urgent transplantations

Table 3: Recipients demographic and clinical characteristics

	Older group ≥80 years (30 pts)	Younger group ≤40 years (60 pts)	p
Age (Years)	52.5 ± 9.4	46.7 ± 10.5	0.012
Gender (Male/Female)	20/10	44/16	NS
Indication for OLT			
Post-necrotic cirrhosis	16*†	30*†	NS
HCC on cirrhosis	9*†	6*†	0.036
Cholestatic disease	0	6	NS
Alcoholic cirrhosis	1	7	NS
Fulminant hepatic failure	3	4	NS
Colangiocarcinoma	1	1	NS
Others	0	6	NS
UNOS status (3/2B/2A/1)	6/16/5/3	20/23/13/4	NS

*HCV positive patients: 13 in the older donor group and 25 in the younger donor group.
†HBV positive patients: 8 in the older donor group and 19 in the younger donor group.

in UNOS status 1 recipients were performed with livers from older donors. Patients with hepatocellular carcinoma (HCC) received a graft more frequently from older than from younger donors. In contrast, no differences were found for the other underlying diseases.

Hepatic function recovery and hospital stay

The post-operative course of serum levels of transaminases, total bilirubin and prothrombin time are shown in Figure 1. Although slightly higher in the patients transplanted with livers from older donors, the serum

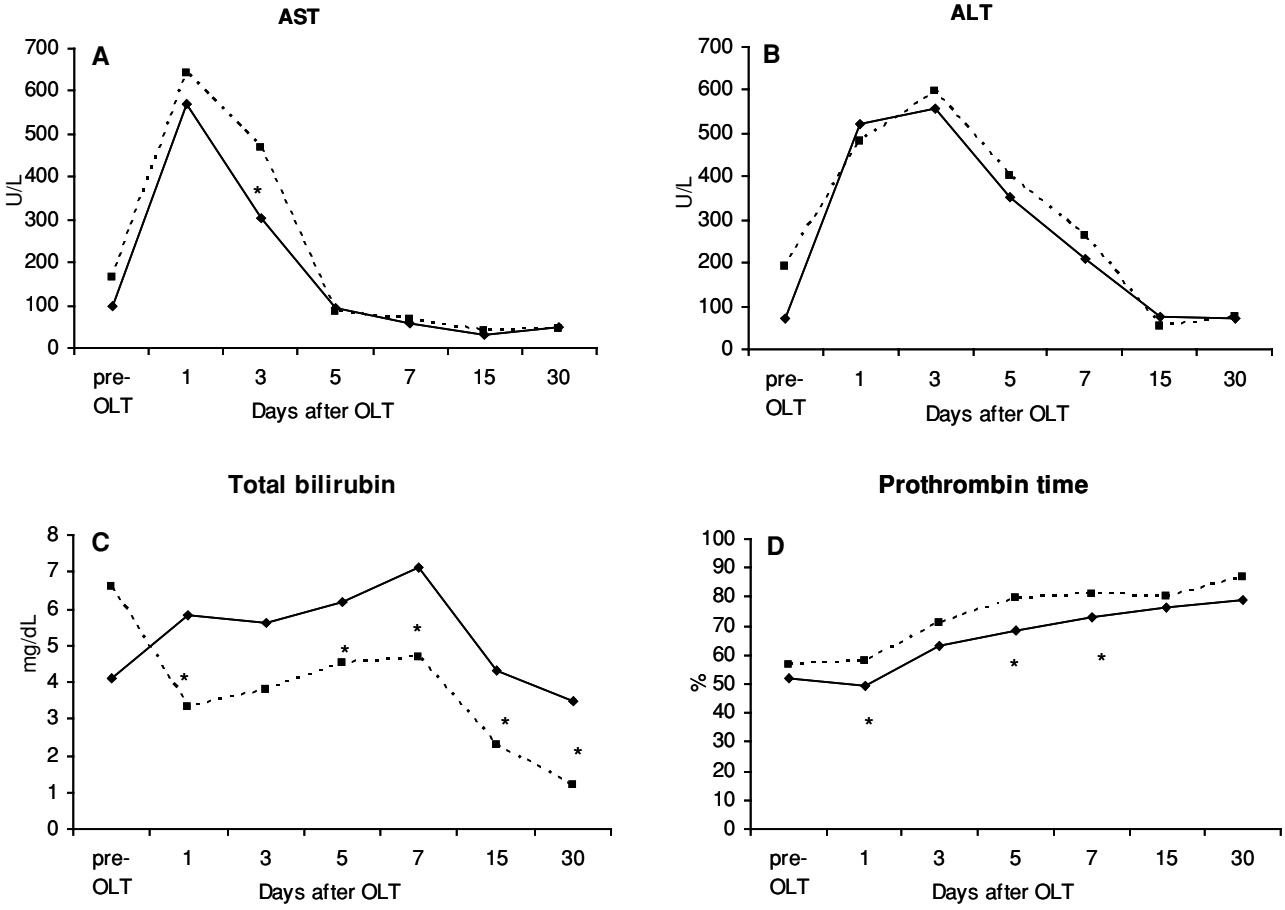

Figure 1: Serum levels aspartate-aminotransferase (AST) (A), alanine-aminotransferase (ALT) (B), total bilirubin (C), and prothrombin time (D) in the first post-operative month in the 60 patients transplanted with grafts from donors ≤40 years (dotted line) and in the 30 patients transplanted with grafts from donors ≥80 years (continuous line). *$p < 0.05$.

transaminase levels did not differ significantly between the two groups except in the third postoperative day. Conversely, total bilirubin remained significantly higher in the older donor than in the younger group throughout the first post-operative month. Significant differences were also found in the PT levels, which were significantly lower in the older than in the younger donor group within the first post-operative week.

The serum levels of γ-GT, alkaline phosphatase, albumin, total protein, creatinine and blood urea nitrogen (BUN), and the urinary output through the first post-operative month were similar in the two groups.

Finally, the daily bile output through the T-tube within the first 7 d after OLT was similar, except in the 3rd post-operative day when it was significantly lower in the older donor than in the younger donor group (184 ± 263 vs. 228 ± 121 cc, $p = 0.012$).

No significant differences were observed between patients transplanted with livers from older and younger donors for the mean post-operative intensive care unit stay (4.7 ± 2.3 vs. 5.1 ± 7.4 d) and for the total hospital stay (19 ± 5.5 vs. 21.9 ± 14.3 d).

Post-operative complications (Table 4)

No significant differences were found between the two groups for acute rejection episodes requiring treatment and nonischemic biliary stenosis. It is important to note that no hepatic artery thrombosis and primary graft dysfunction including both IPF and PNF occurred in the older group.

The rate of re-transplantation was not significantly different: in the younger donor group, the cause for urgent re-transplantation was the occurrence of PNF, while in the older donor group, the only case was related to a rare technical complication represented by the stenosis of the caval anastomosis in the piggy-back procedure.

Graft survival and patient survival (Figures 2 and 3)

Median follow-up was 30.8 months (range: 3.2–52.0 months) in the older donor group and 33.5 months (range: 0.2–60.9 months) in the younger donor group. Transplantation of octogenarian donor livers was associated with a lower overall actuarial patient survival ($p = 0.041$) (Figure 2, lower panel), while graft survival was not significantly influenced (Figure 2, upper panel). Interestingly, no differences were found when the two groups were compared at 3 and 6 months after transplantation: patient survival was 100% and 93.3% in the older donor group and 96.7% and 96.7% in the younger donor group, respectively; similarly, at 3 months and 6 months after transplantation, graft survival was 96.7% and 90% in the older donor group and 90% and 90% in the younger donor group, respectively.

We also evaluated the graft and patient survival of the 13 HCV-positive recipients receiving octogenarian grafts and of the 25 HCV-positive recipients receiving younger grafts. As shown in Figure 3, while graft survival was not significantly different between the two groups (upper panel), patient survival was significantly lower in HCV-positive patients transplanted with older grafts (at 4 years: 40 vs. 81.7%, $p = 0.05$, lower panel).

To exclude a potential selection bias in choosing the control population, the OLTs using donors aged <40 years old and not included in the control group were analyzed. No differences were found in graft survival (at 3 years: 80.6 vs. 80.7%) and patient survival (at 3 years: 87.3 vs. 84.4%).

Causes of post-transplant death (Table 5)

A greater percentage of patients died in the group transplanted with older donors (9/30; 30%) as compared with the younger donor group (7/60; 11.7%) ($p = 0.064$). The causes of death were heterogeneous in both groups. It is worthy of note that the most frequent cause of death in the older donor group was cirrhosis due to hepatitis

Table 4: Post-operative complications

	Older group ≥80 years (30 pts)	Younger group ≤40 years (60 pts)	p
Acute rejection (<30 d)	5 (16.7%)	10 (16.7%)	NS
Non-ischemic biliary stenosis	2 (6.7%)	3 (5%)	NS
Hepatic artery thrombosis	0	2 (3.3%)	NS
Initial poor function	0	0	NS
Primary graft nonfunction	0	2 (3.3%)	NS
HCV recurrent hepatitis*	10/13 (76.9%)	17/25 (68%)	NS
Re-transplant	1 (3.3%)	6 (10%)	NS
Primary graft nonfunction	0	2	
Biliary necrosis	0	1	
Chronic rejection	0	1	
Hepatic artery thrombosis	0	2	
Anastomotic caval stenosis	1	0	

*Histologically proven.

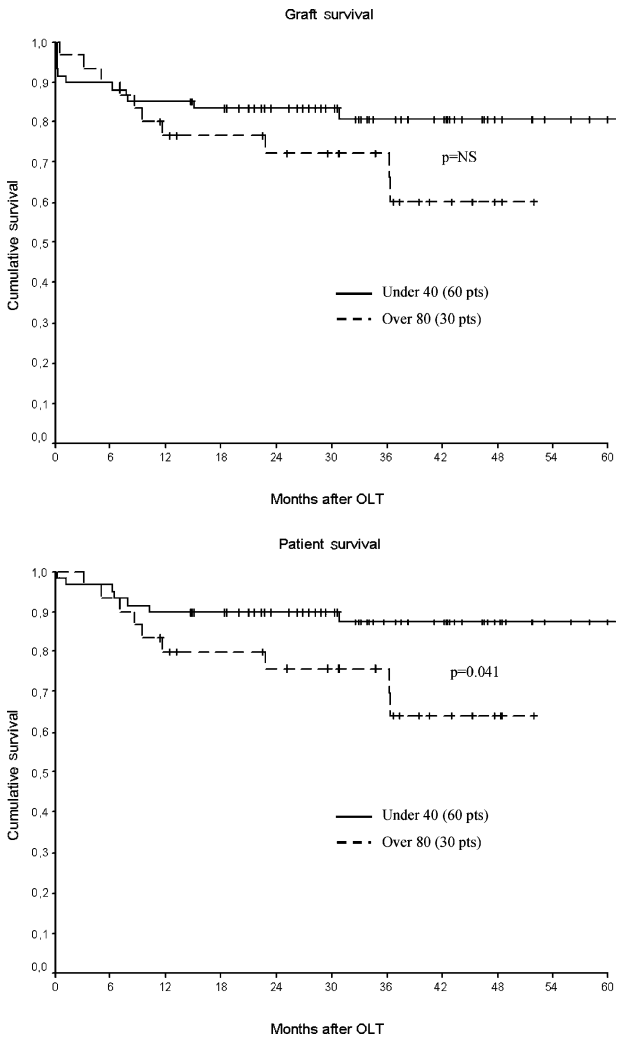

Figure 2: Graft survival (upper panel) and patient survival (lower panel) in the older and younger donor group.

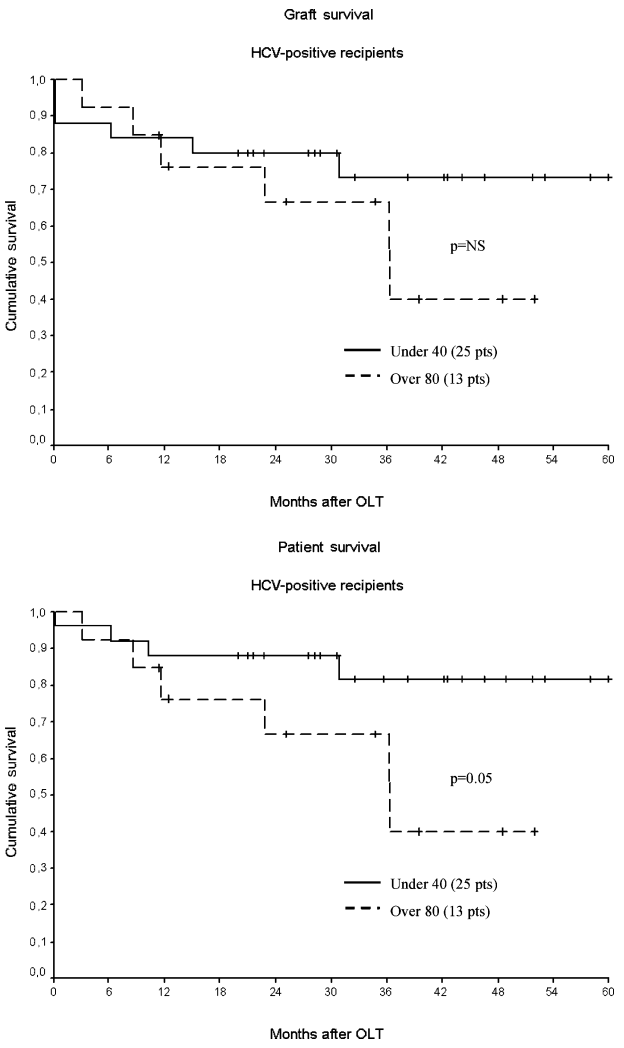

Figure 3: Graft survival (upper panel) and patient survival (lower panel) in the HCV-positive recipients who received octogenarian (13 pts) or <40-year-old grafts (25 pts).

C recurrence (5/9, 55.5%). Interestingly, while the histologically proven hepatitis C was similar in the two groups (10/13, 76.9% vs. 17/25, 68%), the mortality related to hepatitis C was greater in the older than in the younger donor group (5/13, 38.5% vs. 2/25, 8%; $p = 0.063$). Moreover, the time of recurrence from OLT was shorter in octogenarian than younger donors (6.3 ± 4.4 vs. 10.1 ± 6.9 months), although this difference did not reach statistical significance.

Discussion

Aging is associated with a series of pathophysiological changes in all the organs and tissues of the body; however, the liver appears to be less affected by the aging process than other organs such as the heart, the lungs and the kidneys (27). Although a decrease in the functional hepatic mass occurs in the elderly, the liver cells themselves are changed little with advancing age (28). Aging induces several alterations in hepatic function, including protein synthesis, drug metabolism and biliary secretion (28), but the consequences of these changes in healthy aging appears to be minimal because they are counterbalanced by the liver's huge functional reserve, its regenerative capacity and the dual blood supply (29). Older livers are thus likely to be less able to adapt under stress than are livers of younger individuals, but the overall hepatic function is well preserved in healthy aging subjects (29).

These observations represent the biological rationale for expanding the donor pool by transplanting livers from elderly individuals. However, donor aging is still a controversial matter and several concerns have been raised against

Table 5: Causes of death in the liver recipients

No.	Group	Donor age	Follow-up (months)	Cause of death
1	Old	87	36.2	Hemoperitoneum
2	Old	81	8.6	Recurrent HCV hepatitis
3	Old	80	7.0	Recurrent colangioca
4	Old	83	9.5	Sarcoma of Kaposi
5	Old	81	4.9	Lung metastasis of HCC
6	Old	93	11.6	Recurrent HCV hepatitis
7	Old	80	3.2	Recurrent HCV hepatitis
8	Old	81	36.4	Recurrent HCV hepatitis
9	Old	85	22.8	Recurrent HCV hepatitis
1	Young	30	10.3	Recurrent HCV hepatitis
2	Young	26	0.2	Neurological accidents
3	Young	32	6.5	Hepatic artery thrombosis
4	Young	28	6.3	Recurrent HCV hepatitis
5	Young	37	7.9	Multiple organ failure
6	Young	36	1.1	Myocardial infarction
7	Young	19	30.9	Myocardial infarction

the policy to transplant livers from very old donors, based on the evidence that their use is hampered by the higher risk of post-operative complications (12), mainly when associated with long ischemic periods and steatosis (13–16), and by the greater risk of transmission of occult tumors (17,18). Moreover, the lack of a generally accepted upper age limit for donor acceptance leads some transplantation centers to discard a priori livers from septuagenarian and octogenarian individuals.

This large retrospective, case–controlled study clearly shows that livers from octogenarian donors can be used safely for liver transplantation because the post-operative complication rate, early (6 months) graft and patient survivals are similar to those observed in younger donors.

No significant differences were found between the two groups for hepatic artery thrombosis, primary graft dysfunction including PNF, IPF, nonischemic biliary stenosis and acute rejection episodes.

Although an unusually high incidence of arterial complications by transplanting septuagenarian liver donors has been reported (19), graft loss caused by technical complications should not be expected with a greater frequency when using older livers. Indeed, even if the celiac axis may be involved with atherosclerosis (30), the hepatic arterial tree is generally spared even in the elderly (5). Interestingly, in the present study, no hepatic artery thrombosis occurred in the 30 recipients of livers harvested from the older donor group. Several reports have suggested a correlation between the incidence of PNF/IPF and advanced donor age (12,31). In contrast, we did not observe any episode of PNF/IPF in the 30 octogenarian donor livers. However, it should be noted that the serum total bilirubin levels were significantly greater in the patients transplanted with grafts from older donors throughout the first post-operative month. The cause of this prolonged, although mild, cholestasis in octogenarian grafts remains undetermined. We did not find significant differences between the two groups in the incidences of acute rejection, nonischemic biliary stenosis, FK and cyclosporine toxicity, renal failure necessitating dialysis and levels of immunosuppressive drugs. In contrast, a relation close to statistical significance using an ANOVA analysis for repeated measures was found between the length of cold ischemia and the post-operative bilirubin levels in the octogenarian graft group, but not in the group of OLTs performed with younger donors (data not shown). Thus, the cholestasis observed in the older donor group may reflect a greater sensitivity to ischemic injury.

An explanation for the good results of the liver transplantation using octogenarian donors likely resides in the careful selection policy adopted by our centers as shown by the significantly higher percentage of donor livers discarded among the older than younger donors (48.2 vs. 14.3%, $p < 0.001$).

Although no definite cut-off levels were used to identify hemodynamic, laboratory and histologic parameters for excluding the donor in the present retrospective study, the attitude of the surgeons emerged in the careful evaluation of the older donors by searching for liver diseases and solid tumoral lesions. Moreover, it is likely that surgeons are more prone to refuse the older than the younger donors when risk factors for pNF and lpF are present.

The habit of performing a liver biopsy in almost all octogenarian donors led us to identify and discard livers with moderate to massive steatosis and HCV-related cirrhosis, which are expected to have a higher prevalence in the older population (28). Moreover, with the suspicion of undetected malignancies, which could be more frequent among older donors, the guidelines of our centers include a careful donor medical history and evaluation of blood tests, a complete examination of all thoracic and abdominal solid organs and all other parts of the body they have access to during harvesting, and a rapid histologic evaluation when a suspicious nodule or lymphoadenopathy is found. Although this policy cannot detect small tumors and micrometastases with certainty, we were able to exclude four patients because of previously unrecognized malignancies.

The other key factor to success with older grafts appears to be in maintaining the preservation time to as short as possible. Indeed, among all the pre- and peri-operative data analyzed in this study, the cold ischemia time was the only parameter, which proved significantly different between the two groups. These data likely reflect the habit of starting the recipient surgery as soon as possible after the donor operation to minimize cold preservation, regardless of the inconvenience. Several previous clinical and experimental observations support this policy (3,6,32–34). Specifically,

Wall et al. (5) reported good clinical results by maintaining a mean preservation time of about 4 h with the maximum of 6 h. Conversely, in the Pittsburgh study (32), the livers from donors aged 60–79 years, which had a longer preservation time (12.8 h), showed a higher rate of graft failure from ischemic injury compared with younger grafts.

Our results confirm and extend the observations of Romero et al. (4), who disclosed the possibility of using octogenarian donors, reporting the first series of four patients. In their study, the donors were hemodynamically stable, with an ICU stay shorter than 24 h, the cold ischemia time was limited, ranging from 4 to 8 h and 40 min, and mild macrovescicular steatosis was present in one graft. Post-transplantation evolution and follow-up were uneventful without primary dysfunction and/or vascular complications.

In the present study, the long-term patient and graft survival was significantly lower in individuals transplanted with octogenarian donors. The analysis of the causes of death which occurred in patients transplanted with older donors could be helpful in explaining this difference. First, two of the nine deaths were caused by the recurrence of malignancies, presumably reflecting the attitude to allocate the so-called 'marginal livers' to high-risk neoplastic recipients (cholangiocarcinoma in one patient and large-diameter monofocal HCC at the time of surgery in the other patient). The significantly higher prevalence of candidates with tumors in the older donor group than in the younger group supports this assumption, as also reported by other authors (21). Thus, the mortality in the older donor group may, at least in part, reflect the recipient selection policy more than a different outcome of the older grafts.

Another important issue is the observation that the most frequent cause of death in the older donor group was cirrhosis due to hepatitis C recurrence. Interestingly, while the histologically proven hepatitis C was similar in the two groups, the mortality related to hepatitis C was greater in patients with octogenarian donors. Accordingly, the long-term survival of HCV-positive patients transplanted with octogenarian grafts was lower compared with those receiving younger grafts. These findings confirm recent observations in a limited number of patients showing that increasing donor age adversely affects the long-term results of liver transplantation for hepatitis C (35,36) and may have important implications for donor organ allocation, suggesting that recipients with hepatitis C should not, when feasible, receive grafts from very old donors.

The selection of the appropriate recipients for the older livers remains an open question. In the past, marginal grafts were used in seriously ill patients, resulting in a poor OLT outcome. This attitude has been changing over the past decade and marginal grafts, including very old grafts, are transplanted, whenever possible, into clinically stable good risk recipients (37). In the present retrospective study, the octogenarian grafts were allocated more frequently to patients with HCC likely reflecting our general attitude to match older donor livers with a peculiar type of 'marginal recipients', who often have stable clinical conditions. As expected, octogenarian grafts were also given more frequently to older recipients; however, it should be noted that most of them were also HCC patients.

Other evidence emerging from our data suggests that this recipient selection policy could be too restrictive. Indeed, the good results observed with octogenarian donors were not related to the selection of recipients in a better clinical condition as we did not find any difference in the allocation of older and younger donor livers according to the recipient UNOS status. Interestingly, the functional recovery of the five status 2A patients transplanted with older grafts was satisfactory and the only death was related to pulmonary metastases of HCC. Moreover, even three patients with fulminant hepatic failure were successfully transplanted with octogenarian grafts. Although the small number of patients does not make it possible to reach any conclusive statement, these data suggest that even very old grafts, when carefully selected, may be safely allocated to sick recipients.

In conclusions, older donors have become a valuable and growing part of the total donor pool and this study clearly indicates that octogenarian livers can guarantee a normal early functional recovery after transplantation, bearing firmly in mind that careful donor evaluation and a short cold ischemia time are needed to avoid additional risk factors for poor outcome. Thus, donors aged 80 years and over should always be evaluated and carefully selected for OLT. However, hepatitis C recurrence occurs and leads to cirrhosis and death more rapidly in octogenarians grafts. With this in mind, we believe that the allocation policy of these grafts to the recipients may be reconsidered taking into account the poor long-term outcome when transplanted in patients with hepatitis C. Finally, our data also may raise the issue that providing certain criteria are respected, there are no age limits in using livers successfully for transplantation.

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