

Liver transplantation in patients over 60 years of age

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Abstract Liver transplantation was previously only offered to patients under 60 years of age. We have analyzed the outcome after acceptance on the waiting list and after liver transplantation of patients over 60 years old. A total of 150 patients over 60 years old were listed for a first liver transplantation during 1990–1998. The annual number increased throughout the period. Primary biliary cirrhosis, primary sclerosing cholangitis, and acute hepatic failure were the most frequent diagnoses. A total of 119 patients received a first liver allograft. The patient 1-year survival was 75 % and 3-year survival 62 %, which was not significantly lower ($P = 0.21$) than that of the younger patients. When correcting for year of transplantation, the survival was, however, moderately but significantly lower than among the younger patients. Survival among those > 65 years ($n = 38$) did not differ from that of

patients 60–65 years of age ($n = 81$). We conclude that an increasing number of patients over 60 years old can be listed for liver transplantation and receive a liver allograft with highly satisfying results.

Key words Liver transplantation · Older patient

Introduction

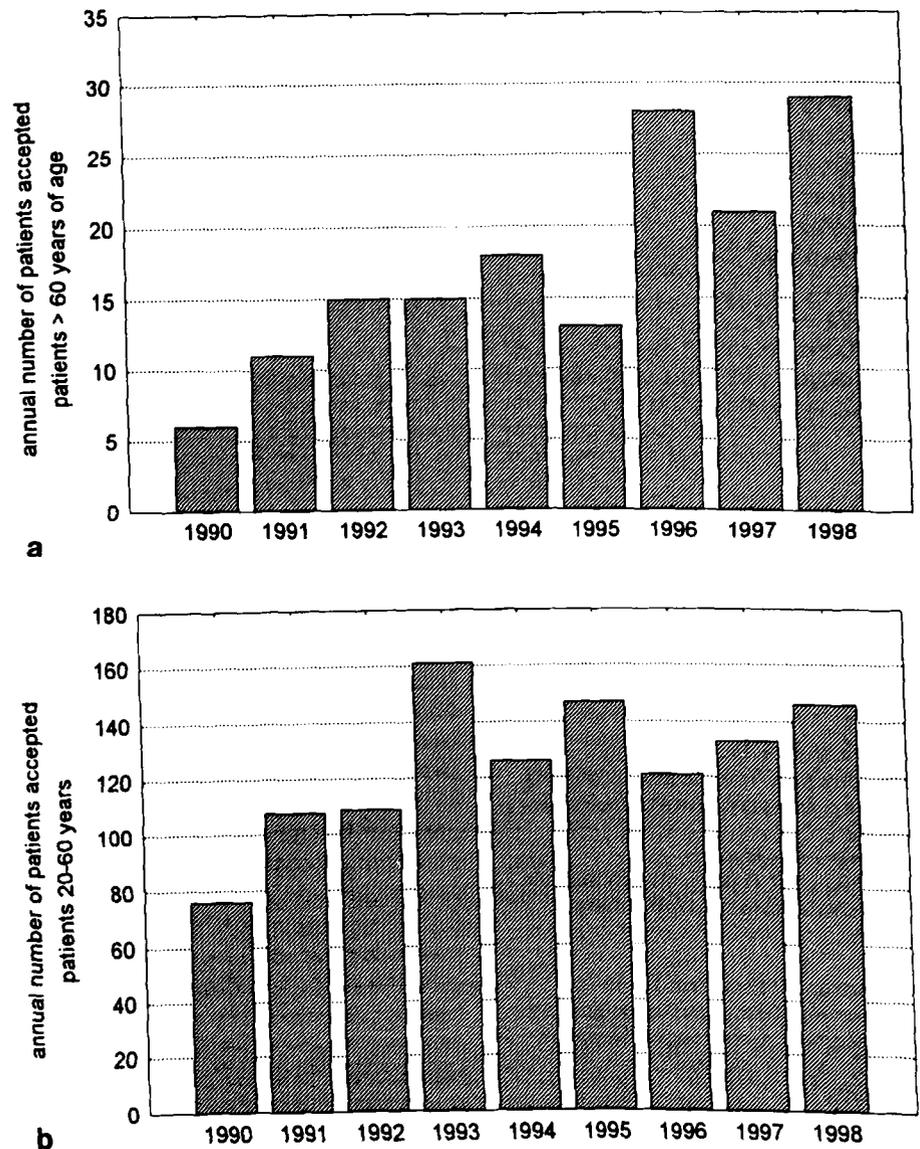
Liver transplantation for acute and chronic liver disease has become an established procedure with highly satisfying results. The number of liver allograft recipients increased in most regions until the early or mid 1990s. Since then, organ shortage has limited the number of transplantations, and the waiting lists have increased in most countries [4, 5].

The prevalence of chronic liver diseases increases with age. Terminal liver failure due to primary biliary

cirrhosis, alcoholic cirrhosis, and autoimmune cirrhosis [3, 4, 8] are more frequently seen in the elderly. Traditionally, liver transplantation has been offered to patients under 60 years of age. An increasing number of patients above this age has, however, been accepted on the waiting list and have received a liver allograft [1, 9]. The results following liver transplantation in recipients over 60 years old have been reported to be acceptable [10, 11].

The aim of the present study was to compare the outcome of older recipients vs younger recipients, both af-

Fig. 1 Number of patients over 60 years of age (a) and between 20 and 60 years old (b) accepted for liver transplantation in the Nordic countries 1990–1998



ter being listed for liver transplantation and following liver transplantation.

Patients and methods

All patients listed for liver transplantations in the Nordic countries (Denmark, Finland, Iceland, Norway and Sweden) have been recorded prospectively in the Nordic Liver Transplant Registry (NLTR) since January 1, 1990. Liver transplantations were performed in Copenhagen, Gothenburg, Helsinki, Oslo, and Stockholm throughout this period. Liver transplantations were also performed in Aarhus, Denmark, during 1993–1994 and in Uppsala, Sweden, in 1994–1997 in a joint program with the liver transplantation team at Huddinge, Stockholm.

NLTR comprises data on all recipients at the time of acceptance, at transplantation, and during life-long follow-up. Donor data are also recorded. Data are entered by the individual trans-

plant center through computers which are on-line with Scandia-transplant. Since November 1994, NLTR has been integrated into the Scandiatransplant computer system at Skejby Hospital, Aarhus, Denmark.

Data on all recipients over 20 years of age at acceptance have been retrieved from NLTR. The patients were categorized as 'older' – over 60 years of age at the time of acceptance on the waiting list, or 'younger' – between 20 and 60 years of age at the time of acceptance.

Statistical analysis

The survival probability of patients was determined by the Kaplan-Meier method and compared by means of the Cox regression analysis. Calculations were performed using Statistica, version 4.5 for Windows. Comparison of variables was performed using the Yates corrected chi-square test or Mann-Whitney U-test when appropriate. For all tests, a *P* value of < 0.05 was considered significant.

Table 1 Age distribution of 150 patients over 60 years old at acceptance for liver transplantation

	<i>n</i>	
60–62 years	54	36%
62–64 years	42	24%
64–66 years	21	14%
66–68 years	14	9%
68–70 years	13	8%
> 70 years	6	4%

Table 2 The most frequent diagnostic groups among older and younger patients (*HCV* hepatitis C virus)

	> 60 years	20–60 years
Primary biliary cirrhosis	50 (33%)	141 (13%)
Primary sclerosing cholangitis	20 (13%)	177 (16%)
Acute hepatic failure	7 (11%)	161 (14%)
Alcoholic cirrhosis	13 (8%)	136 (12%)
Malignant diseases	11 (7%)	104 (9%)
HCV cirrhosis	8 (5%)	61 (5%)
Autoimmune hepatitis – cirrhosis	6 (4%)	45 (4%)

Results

A total of 1351 patients over 20 years old were accepted for liver transplantation in the Nordic countries during the 9-year period 1990–1998. Of these, 150 (11.1%) were over 60 years of age at the time of acceptance, while 1201 (88.9%) were between 20 and 60 years. The number of patients over 60 years old has increased markedly, and during the last 3 years, 'older' patients have comprised 13%–15% of all patients accepted on the waiting list (Fig. 1). There were 95 women and 55 men over 60 years old who were accepted. The age distribution of the patients over 60 years old at acceptance is given in Table 1. The distribution of patients as to blood type ABO was similar among the older and younger patients.

Table 3 Mean and median values of biochemical parameters at acceptance

	> 60 years of age		20–60 years of age		<i>P</i> value
	Mean	Median	Mean	Median	
Creatinine ($\mu\text{mol/l}$)	120	84	110	81	0.26
Prothrombin time (% of normal)	58	55	59	50	0.14
Albumin (g/l)	25.4	25.0	27.7	26.9	0.12

Table 4 Percentages of patients with potential risk factors at acceptance

	20–60 years of age	> 60 years of age	<i>P</i> value
History of encephalopathy grade III or IV	15.7%	11.2%	0.14
At acceptance:			
Hemodialysis	6.2%	5.0%	0.18
Creatinine > 200 $\mu\text{mol/l}$	9.6%	9.4%	0.45
Ventilator	8.6%	3.3%	0.04

There were considerable differences between the centers as 'older' patients comprised only 2.2% of the accepted patients in Oslo, 8.8% in Copenhagen, 13.2% in Stockholm, 15.5% in Helsinki, and 17.3% in Gothenburg.

Diagnosis

The most frequent diagnoses of the older patients were primary biliary cirrhosis, primary sclerosing cholangitis, and acute hepatic failure (Table 2). Compared with the younger patients, relatively fewer patients with alcoholic cirrhosis were accepted for transplantation.

Status at acceptance

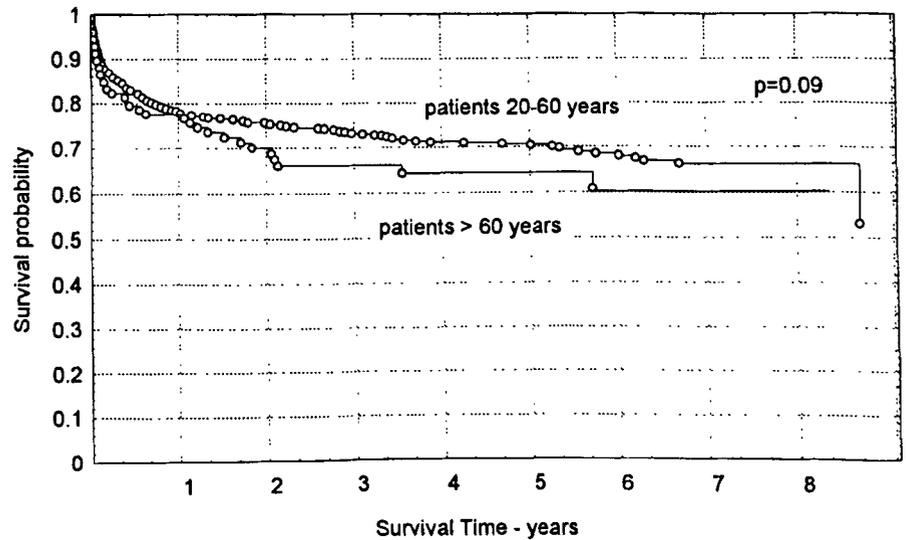
It can be seen from Table 3 that mean and median values of creatinine, bilirubin, albumin, and coagulation factors did not differ significantly between the younger and the older recipients. The percentage of patients with creatinine above 200 $\mu\text{mol/l}$ was also similar (9.4% and 9.3% for older and younger recipients, respectively).

From Table 4 it can be seen that significantly more of the younger patients had a history of severe encephalopathy (grade III or IV). Similarly, more of the younger patients were in need of hemodialysis or a ventilator at the time of acceptance.

Outcome after listing

Among the older patients, 119 (81.2%) received a first liver allograft, 13 (8.0%) were permanently withdrawn from the waiting list, and 18 (10.6%) died while on the waiting list. Significantly fewer of the younger patients died on the waiting list ($n = 80$, 6.7%, $p = 0.04$), but

Fig. 2 Survival of patients 20–60 years (younger) vs patients over 60 years old (older)



more of these younger patients were permanently withdrawn from the waiting list ($n = 138$, 11.5%, $p = 0.04$).

Outcome after transplantation

One-year survival among the older patients was 75% and 3-year survival, 62%. It can be seen from Fig. 2 that the survival rates were comparable and not statistically significantly different from that of patients between 20 and 60 years of age. As most of the older patients received a transplant during the last 4 years of the period, separate survival curves for both patient groups for these 4 years are presented in Fig. 3. It can be seen that the 1-year survival was similar, but 2- and 3-year survivals were poorer among the older recipients.

The survival of patients over 65 years ($n = 38$) of age was not significantly different from that observed among patients between 60 and 65 years ($n = 81$) (Fig. 4).

Men seem to do slightly (not statistically significant) better on a short-term basis than women (for patients over 60 years of age). The 3-year survival was, however, not different between male and female liver allograft recipients over 60 years old at the time of acceptance. The 1-year survival in the four most important diagnostic groups among older and younger recipients is given in Table 5.

Retransplantations were performed more rarely among the older than among the younger patients (6.8% vs 9.5%, respectively, $P = 0.3$).

Discussion

In the Nordic countries there has so far only been a moderate shortage of donor livers. Patients with blood

type 0 have a slightly higher mortality on the waiting list than do patients with blood type A [10]. Combined with a significantly longer waiting time for blood type 0 recipients, this probably signals a significant, though moderate, shortage of blood type 0 livers.

With such a good donor liver availability, it is not surprising that an increasing number of older patients with advanced liver disease are offered liver transplantation. The increase is considerable, and it should be emphasized that every sixth adult patient receiving a liver allograft is over 60 years old at the time of transplantation. In most centers, there is no longer any obvious 60-year upper limit for accepting patients for liver transplantation. There are considerable differences between the transplant centers, signalling that more older patients might be offered this treatment.

The overall survival rates are absolutely satisfactory, but the 3-year survival is poorer among the older patients when correcting for year of transplantation. The 3-year survival rates among patients undergoing transplantation during 1995–1998 were 65% vs 80%. Even though this difference is considerable, a 3-year survival of 65% in patients over 60 years old must be considered satisfactory. The relatively high survival rates among older recipients most probably also reflect the more rigorous selection of patients, as high-risk patients over 60 years old are not accepted to the same extent as are younger patients.

There were only slightly fewer high-risk patients among the older recipients accepted for the waiting list. The only statistically significant difference found was that fewer of the older patients were on a ventilator when accepted for transplantation. Quite surprisingly, risk factors like hemodialysis at acceptance, history of severe encephalopathy, and significantly increased creatinine level did not differ at all between younger and

Fig. 3 Survival of patients 20–60 years (younger) vs patients over 60 years old (older) for patients undergoing transplantation during 1995–1998

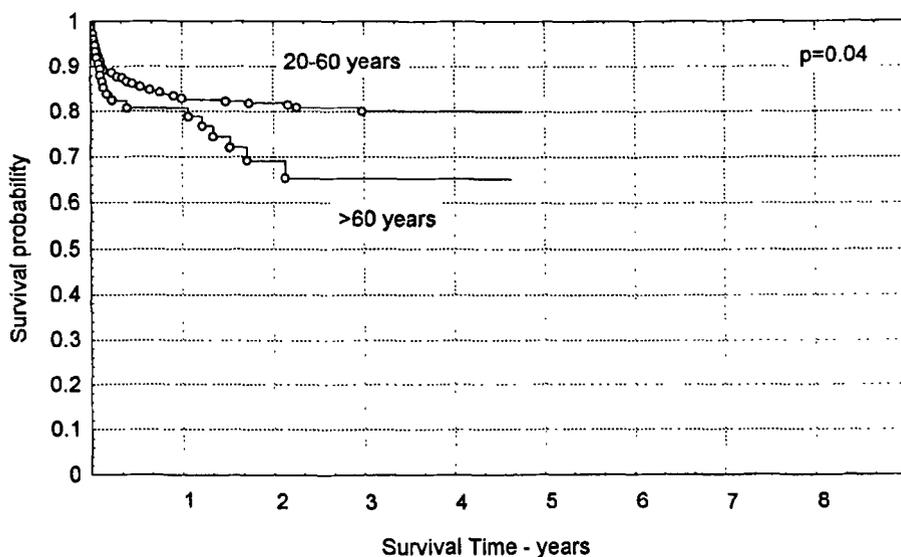
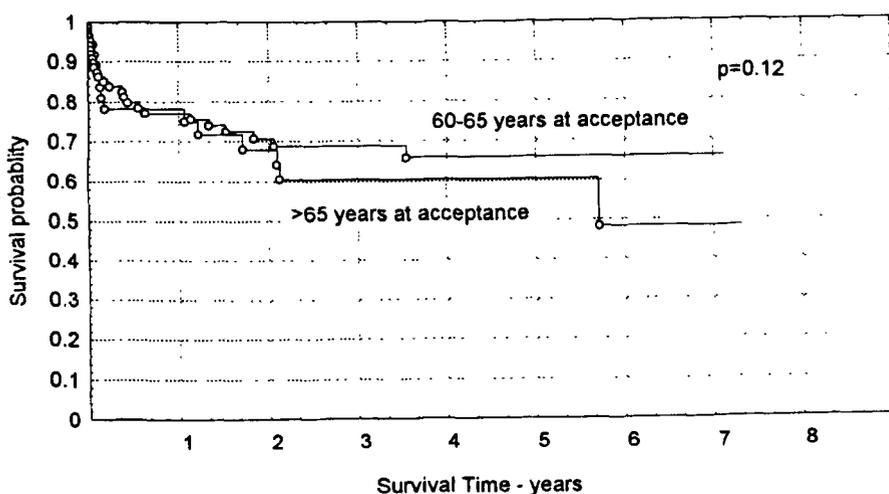


Fig. 4 Survival of patients over 65 years old vs patients aged 60–65 years



older patients. There were also non-significant differences in biochemical parameters like creatinine, coagulation factors, and albumin at acceptance, indicating that the older recipients did indeed have severe liver disease.

The selection is quite obvious for older patients with alcoholic liver cirrhosis with a 1-year survival of 100%. Patients with acute hepatic failure and primary biliary cirrhosis did significantly more poorly than younger patients with the same diagnosis, while older patients

with primary sclerosing cholangitis had a survival which was highly comparable to that of the younger patients.

With the donor organ availability we have had in the Nordic countries during this 9-year period, it seems highly justified to accept patients over 60 years of age for liver transplantation. A strict selection of patients is obviously necessary in order to maintain satisfactory results in this age group.

Table 5 One-year survival among older and younger recipients

	> 60 years	20–60 years	P value
Primary biliary cirrhosis	73 %	86 %	0.04
Primary sclerosing cholangitis	83 %	82 %	0.49
Acute hepatic failure	63 %	76 %	0.04
Alcoholic liver cirrhosis	100 %	74 %	0.03

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