

THE EFFECT OF THE VOLUME OF PROCEDURES AT TRANSPLANTATION CENTERS ON MORTALITY AFTER LIVER TRANSPLANTATION

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ABSTRACT

Background For many complex surgical procedures there is an association between a low volume of procedures and an increased risk of death for the patients who undergo the procedures.

Methods We examined the effect of the volume of procedures at transplantation centers on the risk of death after liver transplantation. We analyzed all liver transplantations performed in the United States between October 1, 1987, and April 30, 1994. Because the results for 1987 to 1991 were largely similar to those from 1992 to 1994, we focused on the more recent period.

Results Between January 1, 1992, and April 30, 1994, 47 centers performed 20 or fewer liver transplantations each per year (total, 837 transplantations) and were designated low-volume centers, and 52 centers performed more than 20 transplantations each per year (total, 6526) and were designated high-volume centers. The one-year mortality rate for the low-volume centers was 25.9 percent, as compared with 20.0 percent for the high-volume centers. Thirteen centers, all of which had low volumes, had one-year mortality rates of more than 40 percent. Low-volume centers that were affiliated with high-volume centers, such as pediatric transplantation programs, had results similar to those of the high-volume centers. The one-year mortality rate at unaffiliated low-volume centers was 28.3 percent, as compared with a rate of 20.1 percent for the group of all high-volume centers plus affiliated low-volume centers ($P < 0.001$).

Conclusions As a group, liver-transplantation centers in the United States that perform 20 or fewer transplantations per year have mortality rates that are significantly higher than those at centers that perform more than 20 transplantations per year. Information regarding the outcome of liver transplantation at transplantation centers should be made widely available to the public. (N Engl J Med 1999;341:2049-53.)

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CURRENTLY, organ transplantation is limited by the availability of donor organs. In the United States, there have been small increases in the number of donor organs available. Nonetheless, since 1994, a rapid rise in the number of patients awaiting transplantation has led to longer waiting times and a greater number of deaths each year among patients on waiting lists for transplants. The death of a patient soon after transplantation also represents the loss of an organ that might have saved another patient's life.

In 1994, Hosenpud et al.¹ analyzed the effect of the volume of procedures at transplantation centers on survival after cardiac transplantation. They found that the risk of death was 33.1 percent higher 12 months after transplantation in centers that performed fewer than nine transplantations per year than in those that performed nine or more procedures. A multivariate analysis demonstrated that the risk of death was independent of differences in the characteristics of the patients from center to center. We used the same methods to examine the effect of the volume of procedures on the risk of death after liver transplantation.

METHODS

We analyzed all liver transplantations performed in the United States between October 1, 1987, and April 30, 1994. We excluded recipients of partial liver transplants from living donors and patients who underwent multiorgan transplantations, in which the liver and other organs from a single donor are transplanted into one recipient. The data were verified by the individual transplantation centers and organ-procurement organizations in conjunction with the *1997 Report of Center-Specific Graft and Patient Survival Rates*,² a study of the outcome of all solid-organ transplantations conducted under the auspices of the Health Resources and Services Administration of the Department of Health and Human Services.

To estimate the effect of the volume of procedures at a center on the risk of death after transplantation while controlling for differences among centers in the donors' and recipients' characteristics, we used a generalized additive model, an extension of standard logistic regression.³ This model is a useful exploratory tool for obtaining simultaneous estimates of the effects of covariates that may be nonlinear. Many of the donor and recipient covariates included in the model were used in the analysis of liver-transplantation outcomes in the *1997 Report of Center-Specific Graft and Patient Survival Rates*.² The list of covariates included characteristics of the recipients (the number of previous transplantations, age, race, diagnosis, medical condition at the time of transplantation, the serum creatinine concentration at transplantation, and the year of transplantation) and factors related to the donor (age, race, and the duration of cold ischemia).

The outcome measure was the mortality rate one year after transplantation. To determine the relation between the volume of procedures and the risk of death, we determined the average number of transplantations performed per year at each center. The log-transformed value was included as an additional covariate in the generalized additive model; log transformation corrected for the fact that there were only a few centers with very large volumes. An estimate of the effect of the number of procedures performed per year was calculated on the basis of data obtained during two periods: October 1, 1987, to December 31, 1991, and January 1, 1992, to April 30, 1994. Rather than choose arbitrary volume categories

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TABLE 1. CHARACTERISTICS OF THE LIVER-TRANSPLANTATION CENTERS, ACCORDING TO THE AVERAGE NUMBER OF PROCEDURES PERFORMED PER YEAR, 1987–1994.

VARIABLE	≤20 Pro- CEDURES/YR	>20 Pro- CEDURES/YR	TOTAL
October 1, 1987, to December 31, 1991			
No. of centers	61	27	88
No. of transplantations	1946	7677	9623
No. of patients	1738	6622	8360
1-Year mortality (%)	29.9	25.1	26.1
Patients with complete follow-up data at 1 year (%)	99.5	99.6	99.6
January 1, 1992, to April 30, 1994			
No. of centers	47	52	99
No. of transplantations	837	6526	7363
No. of patients	770	5929	6699
1-Year mortality (%)	25.9	20.0	20.7
Patients with complete follow-up data at 1 year (%)	95.9	94.8	95.0

ries, we grouped the centers into two categories on the basis of these analyses.

Many low-volume centers were identified as being closely affiliated with adjacent centers that had high volume; many of these affiliated centers were pediatric programs in separate but affiliated pediatric hospitals. In a preliminary analysis, we found that the outcome was markedly poorer at low-volume centers that were not affiliated with high-volume centers than at all other centers as a group. Therefore, for some analyses, the centers were subcategorized as affiliated or unaffiliated.

To determine the final estimate of the effect of the number of procedures performed per year on the one-year mortality rate, we entered the data for 1992 to 1994 into a multivariate logistic-regression model in which the response variable was the death of the patient within one year after transplantation. In this model, rather than excluding patients with insufficient follow-up, we weighted the data on patients who were not followed up for one year.³ An indicator variable was created for the category of the center as de-

termined from the generalized additive model, and this variable was included in the logistic-regression model along with the donor and recipient covariates. The modal category or mean values were used for covariates with missing data; for example, data on the duration of cold ischemia were missing for 6.7 percent of transplantations, whereas data on other covariates were missing for less than 1 percent.

Because follow-up was not complete, particularly in the case of transplantations performed in 1992 or later, unadjusted mortality rates were calculated according to the Kaplan–Meier method.⁴ All statistical calculations were performed with S-Plus for Windows (version 3.3, StatSci, Seattle) or SAS (version 6.09, SAS Institute, Cary, N.C.) statistical software. In the analysis of the patients' characteristics, the chi-square test was used for categorical variables⁵ and the t-test was used for continuous variables.⁶ Differences in survival curves were compared with the use of the log-rank test.⁷ All reported P values are two-sided.

RESULTS

Table 1 shows the number of transplantation centers and the number of transplantations performed from October 1, 1987, to December 31, 1991, and from January 1, 1992, to April 30, 1994. Between January 1, 1992, and April 30, 1994, 47 centers performed 20 or fewer liver transplantations each per year and 52 performed more than 20 per year. The centers in the low-volume group (20 or fewer transplantations per year) performed 11 percent of all transplantations during this period, whereas high-volume centers (more than 20 procedures per year) performed 89 percent.

The relation between the number of procedures performed per year and the mortality rate one year after liver transplantation from 1992 to 1994, as determined by the generalized additive model, is shown in Figure 1 and closely resembles the findings for the period from 1987 to 1991 (data not shown). During both periods, mortality rates stabilized at centers that performed more than 20 transplantations per

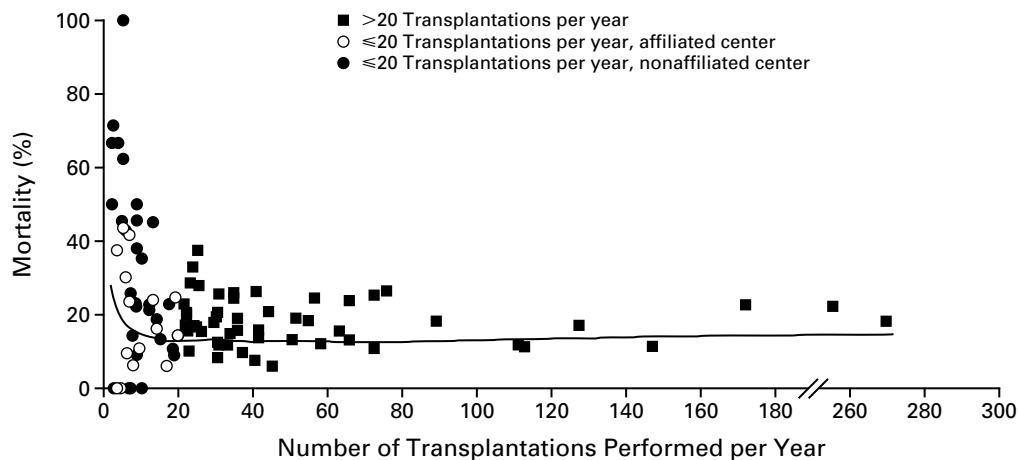


Figure 1. Relation between the Number of Procedures Performed per Year and the Mortality Rate One Year after Liver Transplantation at 99 Centers from January 1, 1992, to April 30, 1994.

An affiliated center was one that was closely affiliated with an adjacent high-volume center.

TABLE 2. RELATION BETWEEN THE NUMBER OF PROCEDURES PERFORMED PER YEAR AND AFFILIATION STATUS AND THE RISK OF DEATH ONE YEAR AFTER LIVER TRANSPLANTATION, 1992–1994.

GROUP	NO. OF TRANSPLANTATIONS	NO. OF CENTERS	1-YEAR MORTALITY %	ADJUSTED ODDS RATIO (95% CI)*
Affiliated centers performing ≤ 20 transplantations per year	309	15	21.8	1.06 (0.74–1.50)
Unaffiliated centers performing ≤ 20 transplantations per year	528	32	28.3	2.08 (1.65–2.61)
Affiliated centers performing > 20 transplantations per year	995	11	18.2	1.11 (0.91–1.35)
Unaffiliated centers performing > 20 transplantations per year	5531	41	20.4	1.00†
Unaffiliated centers performing ≤ 20 transplantations per year	528	32	28.3	2.04 (1.63–2.55)
Affiliated centers performing ≤ 20 transplantations per year plus all centers performing > 20 transplantations per year	6835	67	20.1	1.00†

*Odds ratios were adjusted for the donor's age and race and for the recipient's age, race, diagnosis, number of previous liver transplantations, serum creatinine concentration at transplantation, medical condition at transplantation, and year of transplantation. CI denotes confidence interval.

†This group served as the reference group.

year and increased inversely with transplantation volumes of less than 20 per year. Thirteen centers, all of which had low volumes, had mortality rates of 40 percent or more. Accordingly, using the data for 1992 to 1994, we grouped centers into those that performed 20 or fewer transplantations per year and those that performed more than 20 per year.

We used logistic-regression analysis to estimate the odds of death at one year for transplantations performed during the period from 1992 to 1994 at centers categorized according to the number of procedures per year and affiliation status, after adjustment for the following covariates: donor's age and race and recipient's age, race, diagnosis, number of previous liver transplantations, serum creatinine concentration at the time of transplantation, medical condition at the time of transplantation, and year of transplantation. The performance of affiliated low-volume centers and affiliated high-volume centers was similar, as was the performance of affiliated and unaffiliated high-volume centers (Table 2). In a separate comparison of low-volume centers, the odds of death within one year after liver transplantation at all unaffiliated centers was nearly twice that at all affiliated centers (adjusted odds ratio, 1.97; 95 percent confi-

dence interval, 1.32 to 2.94). Therefore, in the remainder of the analyses, the centers were divided into two groups: unaffiliated low-volume centers and high-volume centers plus affiliated low-volume centers. As compared with the odds of death for the entire group of high-volume centers and affiliated low-volume centers, the odds ratio for death at low-volume unaffiliated centers was 2.04 (95 percent confidence interval, 1.63 to 2.55).

The characteristics of the donors and the liver-transplant recipients are shown in Table 3. Donors and recipients at unaffiliated low-volume centers were younger than those at high-volume centers and affiliated low-volume centers. The percentage of recipients who were less than 18 years of age was similar in the two groups. Recipients at unaffiliated low-volume centers were more likely to be black and less likely to have received a previous liver transplantation. Figure 2 shows Kaplan–Meier estimates of survival at one year. The survival rates were significantly higher ($P < 0.001$) in the group of high-volume centers and affiliated low-volume centers than in the unaffiliated low-volume centers. The difference in mortality rates between the two groups was 6.8 percentage points at 90 days and 8.2 percentage points at 1 year (Table 3).

It has been suggested that the sickest liver recipients may have a higher risk of death if they undergo transplantation at low-volume centers. Using the logistic-regression model, we tested this hypothesis for recipients of a second transplant and for those who were receiving life support at the time of transplantation. Patients who were receiving life support at the time of transplantation had a higher risk of death if they underwent the procedure at an unaffiliated low-volume center rather than at a high-volume center or an affiliated low-volume center (mortality rate, 51.4 percent vs. 39.3 percent; adjusted odds ratio, 2.2; 95 percent confidence interval, 1.25 to 3.74). For recipients of a second or subsequent transplant, the mortality rate was 64.4 percent at unaffiliated low-volume centers, as compared with 41.3 percent at the other centers (adjusted odds ratio, 3.1; 95 percent confidence interval, 0.99 to 9.88). The wide confidence intervals reflect the small number of recipients of a second or subsequent transplant at low-volume centers (31 recipients).

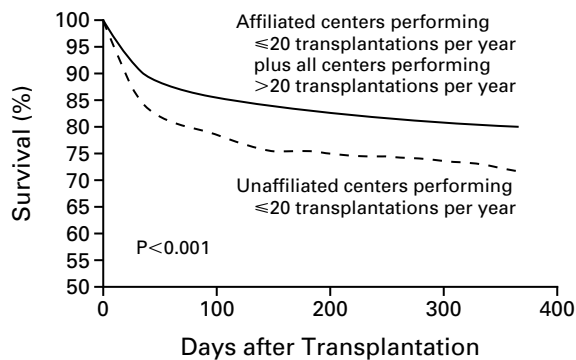
DISCUSSION

We found that, as a group, liver-transplantation centers in the United States that perform 20 or fewer transplantations per year had mortality rates that were significantly higher than those at centers that perform more than 20 transplantations per year. The effect on mortality of the number of procedures performed per year was even greater when low-volume centers that were affiliated with a high-volume center were compared with low-volume centers that were not so affiliated. In the initial analysis, we found that

TABLE 3. CHARACTERISTICS OF LIVER-TRANSPLANT DONORS AND RECIPIENTS, 1992-1994.*

CHARACTERISTIC	AFFILIATED CENTERS PERFORMING ≤ 20 TRANSPLANTATIONS PER YEAR PLUS ALL CENTERS PERFORMING >20 TRANSPLANTATIONS PER YEAR (N=6835)	UNAFFILIATED CENTERS PERFORMING ≤ 20 TRANSPLANTATIONS PER YEAR (N=528)	P VALUE
Donors			
Age — yr	30.7 \pm 0.2	28.6 \pm 0.7	<0.001
Race — no. (%)			
White	5352 (78.3)	384 (72.7)	0.003
Black	782 (11.4)	66 (12.5)	
Other	701 (10.3)	78 (14.8)	
Recipients			
Age — yr	42.0 \pm 0.2	39.8 \pm 0.8	0.004
Age <18 yr — %	14.5	14.4	
Race — no. (%)			
White	5232 (76.6)	380 (72.0)	<0.001
Black	502 (7.3)	67 (12.7)	<0.001
Other	1101 (16.1)	81 (15.3)	
Previous liver transplantation — no. (%)	812 (11.9)	31 (5.9)	0.003
Diagnosis — no. (%)			
Cholestatic liver disease or cirrhosis	1153 (16.9)	85 (16.1)	
Other type of cirrhosis	3854 (56.4)	319 (60.4)	
Cancer	234 (3.4)	13 (2.5)	
Other	1594 (23.3)	111 (21.0)	
Medical condition at transplantation — no. (%)			
Hospitalized in intensive care unit			
Not receiving life support	1554 (22.7)	108 (20.5)	
Receiving life support	986 (14.4)	71 (13.4)	
Hospitalized but not in intensive care unit	1346 (19.7)	114 (21.6)	
Other	2949 (43.1)	235 (44.5)	
Mortality rate — %			
At 90 days	14.1	20.9	<0.001
At 1 yr	20.1	28.3	<0.001

*Plus-minus values are means \pm SE.



No. AT RISK	0	100	200	300	400
Affiliated centers performing ≤ 20 transplantations per year plus all centers performing >20 transplantations per year	6835	5787	5473	5299	4577
Unaffiliated centers performing ≤ 20 transplantations per year	528	405	381	371	344

Figure 2. Kaplan-Meier Estimates of Survival at One Year, According to the Number of Transplantations Performed per Year.

An affiliated center was one that was closely affiliated with an adjacent high-volume center.

a significant number of children underwent transplantation at affiliated low-volume centers and that the results were similar to those at high-volume centers.

The increased risk of death in the unaffiliated low-volume centers did not appear to be an effect of the patients selected. Patients who are in the intensive care unit and those who are receiving life support at the time of liver transplantation have a higher risk of death than do healthier liver-transplant recipients.² The percentages of transplantations that were performed in patients who were receiving life support or were in the intensive care unit at the time of the procedure were similar in unaffiliated low-volume centers and the entire group of affiliated low-volume centers plus all high-volume centers. The outcome of transplantation for these sicker patients was poorer at the unaffiliated low-volume centers. A higher percentage of black patients underwent transplantation at low-volume unaffiliated centers. Black patients have a higher mortality rate after liver transplantation than white patients.⁸ Our analysis adjusted for the potential effect of the recipient's race on the risk of death.

We found that some centers that perform 20 or fewer liver transplantations per year had a low mortality rate. In part, this may reflect statistical variation. It may also reflect other factors that we were unable to measure.

The association between a low volume of procedures and an increased risk of death among patients undergoing complex surgical procedures is well established.^{9,10} It is therefore not surprising that we found an association between the number of procedures performed per year and the outcome of liver transplantation. The responsible factors might include the experience of the center and the experience and skill of the surgeons. In the case of heart transplantation,¹ Hosenpud et al. found no difference in the risk of death among the first 10 patients who underwent transplantation at a center as compared with the next 10 patients, suggesting that the accumulated experi-

ence of the center was not an important factor in determining survival. We have also found that cumulative experience at a liver-transplantation center was not a factor in determining mortality (data not shown).

Is there adequate information to enable physicians to steer their patients away from transplantation centers with high mortality rates? Thirteen centers had mortality rates that exceeded 40 percent, and the rate at one of these centers was 100 percent (Fig. 1). It would be reasonable to assume that, given this information, patients would decide to undergo transplantation at a center with low mortality rates.

Our findings suggest that the information available to patients and referring physicians is inadequate or that regional health care systems may be forcing patients to go to centers with poor results. Information regarding the outcomes of liver transplantation at transplantation centers should be made widely available to the public in a timely manner.

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